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14. ABSTRACT
The development of a new tool to accurately delineate cancer within the prostate is urgently needed to shape the future of PCa workup and biopsy guidance. To provide a more effective, practical tool for clear identification of PCa for biopsy, this IDEA proposal will develop a nano-sized US contrast agent (called a nanobubble – NB) targeted to the prostate specific membrane antigen (PSMA) via a new highly selective ligand. The targeted NBs are similar in structure to clinically used microbubbles (MB) and are clearly visible on clinical US at comparable frequencies of 3-12 MHz. However, in stark contrast to MB which remain in the vasculature, the <200 nm NB size enables them to extravasate into the tumor parenchyma and directly bind to cancer cells. This can result in higher accumulation of contrast at the tumor itself leading to better resolution and detection of PCa. The PSMA-targeted NB has the capacity to revolutionize PCa imaging, since US is so broadly available, low cost, and safe. Importantly, US is already frequently utilized in PCa biopsy procedures, and the same exact equipment and process can be applied for NB imaging, thus lowering cost and expediting development and clinical translation.

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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The development of a new tool to accurately delineate cancer within the prostate is urgently needed to shape the future of PCa workup and biopsy guidance. To provide a more effective, practical tool for clear identification of PCa for biopsy, this IDEA proposal will develop a nano-sized US contrast agent (called a nanobubble – NB) targeted to the prostate specific membrane antigen (PSMA) via a new highly selective ligand. The targeted NBs are similar in structure to clinically used microbubbles (MB) and are clearly visible on clinical US at comparable frequencies of 3-12 MHz. However, in stark contrast to MB which remain in the vasculature, the <200 nm NB size enables them to extravasate into the tumor parenchyma and directly bind to cancer cells. This can result in higher accumulation of contrast at the tumor itself leading to better resolution and detection of PCa. The PSMA-targeted NB has the capacity to revolutionize PCa imaging, since US is so broadly available, low cost, and safe. Importantly, US is already frequently utilized in PCa biopsy procedures, and the same exact equipment and process can be applied for NB imaging, thus lowering cost and expediting development and clinical translation.
The specific objective of this project is to optimize PSMA-targeted nanobubbles for US detection of PCa. Specifically we will: 1) formulate targeted NBs and characterize NB parameters in human PCa lines (e.g. bubble echogenicity and stability, specificity and longevity of cell targeting); and 2) compare the US detection properties of PSMA-targeted NB to untargeted NBs and clinical MB agents (Definity®) in both flank and orthotopic *in vivo* PCa models. This proposal represents the first step in establishing these NB agents as tools for guided biopsies of the future, and will confirm that the NBs can indeed delineate a target lesion of concern more effectively on US than current standard of care. In the long term, biopsies improved by the PSMA-targeted US contrast agents could lead to increased detection of high grade tumors and tumor staging, and lower morbidity.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Ultrasound contrast agent, nanobubbles, microbubbles, PSMA, prostate cancer, imaging, molecular imaging, early detection, biopsy guidance.

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Three specific aims support the project objectives:

Aim 1: Formulate and characterize PSMA targeted NBs (PSMA-1-NB): We will determine the optimal NB formulation parameters once they are functionalized by the PSMA-1 ligand. We seek a stable

formulation that will be successfully targeted to PSMA with high yield. The formulation needs to be visible on US and sustain its signal for at least 1 hr and be 200 nm.

Aim 2: Establishment of NB in vivo performance: The primary objective of this aim will be to characterize and maximize PSMA-1-NB signal at the PSMA positive tumors and minimize in PSMA negative ones. We will compare these to MB performance in the same tumors.

Aim 3: Application of targeted NBs in detection of orthotopic PCa: Because a clinically relevant tumor microenvironment and tumor heterogeneity as well as the delineation of the tumor within the prostate tissue play crucial roles in the outcomes of the proposed imaging technique, it is necessary to carry out an imaging study on an orthotopic model of PCa. This model has been established by the Basilion lab in mice, and we will build upon their extensive knowledge of this model to test the imaging strategy. We will acquire US images and will then utilize 3D whole mouse cryoimaging [52] to determine the efficacy of segmentation of the tumor and prostate tissue.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Proposed Statement of Work (Months 1-12)

In the application, we proposed to focus primarily on formulation and optimization of the nanobubble contrast agents during the first 12 months. During this time, we have accomplished nearly all of the sub-tasks proposed. These are labeled with a green dot (●). The sub-tasks which have a yellow dot (●) are currently underway. We describe the details of our major accomplishments below.

<u>Task 1</u>: Formulate and characterize stable NBs targeted to PSMA receptor (months 1-10)

1a. Develop optimized combination of lipids and surfactants to form NBs (months 1-2) ●
1b. Optimize conditions for fluorescent labeling of NBs (months 1-2) ●
1c. Determine best strategy for targeting NBs to prostate cancer with the PSMA antibody (months 2-3) ●
1d. Formulate stable targeted NBs (months 2-3) ●
1e. Characterize NB properties (months 1-3) ●
1f. Measure NB stability (months 1-3) ●
1g. Refine techniques as needed to achieve optimized NB <100 nm and stable for >1hrs (months 1-4) ●
1h. Carry out acoustic characterization of NBs (months 4-5) ●
1i. Initiate culture of PCa cell lines in collaboration with J Basilion (months 4-7) ●
1j. Confirm PSMA expression on cells (months 4-5) ●
1k. Determine targeted NB attachment on cultured cells under <u>static</u> conditions (months 4-7) ●
1l. Determine targeted NB attachment on cultured cells under <u>flow</u> conditions (months 7-10) ●

1m. Measure NB adhesion using flow cytometry (months 5-9)
1n. Statistical analysis of results and refinement as needed to achieve desired criteria (months 9-10)

<u>Task 2:</u> Evaluate contrast agent properties *in vivo* in flank prostate cancer model in mice (months 11-24)

2a. Prepare and attain IACUC approval for mouse xenograft studies (months 9-11)
2b. Inject tumor cells in flank in male mice in collaboration with J Basilion (months 11-15)
- 5 groups (PCa cell lines, 3 types of bubbles) of n=9 for each endpoint. Total of 126 mice

2c. Carry out biodistribution studies with FMT, ultrasound imaging and ex vivo tissue analysis (months 10-14)
2d. Measure bubble dynamic parameters (months 10-14)

1. Overview of research accomplished pertaining to Task 1

During the past year, we have carried out a substantial amount of work in this area. Our initial efforts focused on optimization of the nanobubble stabilizing shell, which is a critical component which influences the nanobubble longevity and interaction with ultrasound. To carry out these studies, we first examined the effect of two different lipids (DPPC and DBPC) as well as the combination of lipids and lipid to Pluronic ratio on the stability and size distribution of the nanobubbles. We also formulated hybrid lipid and polymer (polyacrylamide)-stabilized nanobubbles and examined their morphology under cryo electron microscopy (cryo-EM), and we examined bubble morphology following exposure to ultrasound, to confirm their size and presence of gas inside of the lipid core. Finally, we studied two different ways of isolating the nanobubble population and removing any bubbles which were larger than 1 micron. Here we refined the centrifugation protocol and we also utilized a set of filters to remove the large bubble population and reduce polydispersity.

Pertaining to synthesis and conjugation of PSMA-1 ligand to the phospholipids, we first confirmed PSMA-1-cys ligand synthesis via MALDI-TOF analysis. We concurrently confirmed conjugation of thiol groups to the commercially obtained DSPE-PEG-maleimide lipids using a standard Ellman's assay, which is used to quantify the number or concentration of thiol groups in a sample. We then confirmed the conjugation of the DSPE-PEG—MAL lipid to the PSMA-1 ligand, also using MALDI-TOF analysis. In addition, the cell lines which we will utilize for *in vitro* as well as *in vivo* work were cultured, and the expression of PSMA was validated using western blotting.

Following the initial fundamental experiments to stabilize nanobubbles and develop and validate the targeting ligand, optimized nanobubbles were decorated with the PSMA-1 ligand. The nanobubble echogenicity, acoustic stability and size were characterized. Optimization of ligand density was carried out in live cells using an ELISA-like assay and the output was analyzed using a fluorescence plate reader. Confirmation of binding in cells was confirmed using fluorescence microscopy as well as a competition binding assay between free PSMA-cys and PSMA-1-conjugated nanobubbles (PSMA-1-NB).

1.1. Lipid acyl chain length improves stability of nano-sized ultrasound contrast agents *in vitro*

Ultrasound contrast agents require additional optimization with respect to their echogenicity, stability and size to make them suitable for cancer molecular imaging in extravascular applications. We had previously developed lipid and surfactant-stabilized perfluorocarbon gas nanobubbles (NB) capable of extravasating the permeable vasculature of tumors in contrast to conventional microbubbles which are too large (1-10 μm) to enter the interstitial space.[1,2] The objective of this set of experiments was to increase the stability of the NBs by optimization of the lipid hydrophobic chain length to improve the bubble shell in-plane rigidity. Specifically, based on previous microbubble literature, we replaced 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC), a 16 carbon chain lipid, with 1,2-dibehenoyl-*sn*-glycero-3-phosphocholine (DBPC), a 22 carbon chain lipid.[3]

Methods**:** Nanobubbles were made by agitation of lipids, Pluronic L10, and glycerol in the presence of C_3F_8 gas. The mass ratio of lipids in the DPPC containing bubbles was 4:1.5:1:1 mg for DPPC, DPPE, DPPA and PEG respectively per vial of bubbles. The mass ratio of lipids in the DBPC containing bubbles was 6.1:2:1:1 mg per vial of bubbles, where DPPC is completed replaced by DBPC. The bubbles were imaged in an acrylamide phantom (**Fig. 1.A**) in PBS via contrast harmonic imaging (Toshiba, 12 MHz, MI 0.1).

Results and Discussion: Increasing the acyl chain length of the most prominent lipid in our formulation significantly improved (p>0.001) the half-life of our nanobubbles from 1.4 minutes to 5.8 minutes (**Fig 1.B-C**). This supports what previous literature has found to be true of microbubbles and shows that the same trends are found in nano-sized bubbles. We hypothesize that the longer chains increase lateral cohesion forces, which increases the bending modulus and decreasing lateral density fluctuations of the bubble.[3] The decreased bending modulus lessens buckling of the lipid monolayer, which prevents dissolution. Additional in depth experiments are required to support this hypothesis.

Conclusions: Increasing length of the acyl chain of the most prominent lipid from 16 to 22 carbons, while maintaining about the same molar ratios of all the lipids in the formulation resulted in a 4-fold improvement in half-life of nanobubbles under near continuous US exposure. Future studies will investigate the effects of acyl chain length on bubble stability and accumulation in cancerous tumors *in vivo*.

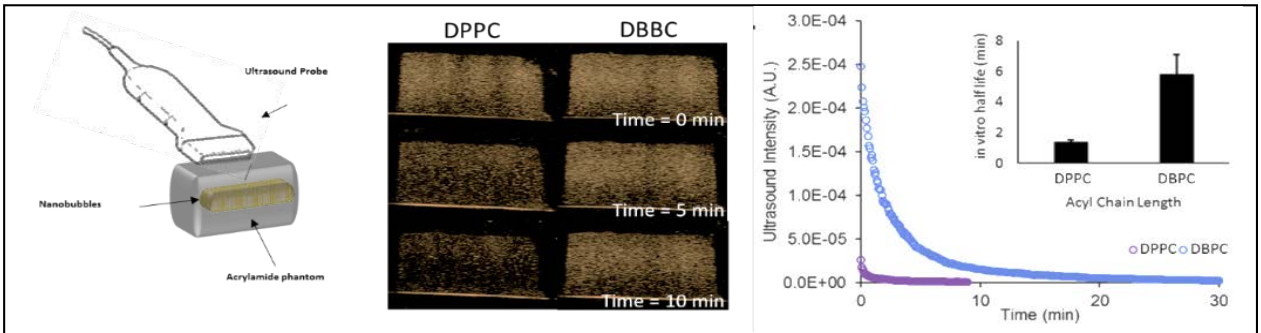


Figure 1. Effect of lipid acyl chain length on nanobubble stability under ultrasound exposure. (A) Schematic of acrylamide phantom used to measure in vitro stability. (B) Typical ultrasound images of nanobubbles at different time points. (C) Representative ultrasound time intensity curves and average half-life of each formulation.

1.2. Effect of the Surfactant Pluronic on the Stability of Lipid-Stabilized Perfluorocarbon Nanobubbles Due to their 1-10 μm size range, microbubbles (MBs) have limited use in cancer detection and treatment. To expand contrast enhanced US capabilities, we have developed sub-

micron contrast agents via the addition of Pluronic, a nonionic triblock copolymer surfactant, to the phospholipid shell stabilizing perfluoropropane (C_3F_8) gas (**Fig 2A**). NBs, with diameter of ~200nm, can take advantage of the EPR effect, extravasate the leaky tumor vasculature and accumulate in tumors. Prior work has shown that bubble echogenicity and stability are, in part, dependent on the surface tension of the stabilizing shell. In this study, we evaluate the effect of Pluronic on surface tension of the lipid films and how its presence in the NB shell affects echogenicity and signal decay at clinically-relevant imaging frequencies.

Methods: Pluronic L10 (MW 3200, PPO/PEO units of 49.7/7.3), at three Pluronic:lipid molar ratios (0.02, 0.2, and 0.4), was incorporated into the lipid film composed of a mixture of DPPC, DPPE, DPPA and DSPE-PEG. Bubble diameter was measured with dynamic light scattering (DLS). The surface tension of each composition was measured using pendant drop tensiometry. To test the effect of Pluronic concentration on bubble stability, NBs with the same Pluronic:lipid ratios were formulated by hydrating the lipid mixture described above with the appropriate Pluronic concentration and exchanging air with C_3F_8. Bubbles were then activated using mechanical agitation and imaged in PBS inside an agarose phantom using a standard diagnostic US scanner (Toshiba Aplio) in contrast harmonic mode at 12 MHz, MI 0.1, and 0.2 frames per second.

Results, Discussion and Conclusions: The incorporation of Pluronic L10 significantly decreased the surface tension, especially at a ratio of 0.2, where this value decreased by 27% ($p < 0.0001$) (**Fig 2 B**). This led to a significant decrease in the signal decay over time resulting in a stability increase of 39% ($p < 0.0001$) (**Fig 2C-D**). The Pluronic had little impact on size; NBs had an average diameter of 208 ± 21.3 nm. Future work will evaluate surface tension effects Pluronic of different PEO-PPO ratios to further optimize the NB formulation.

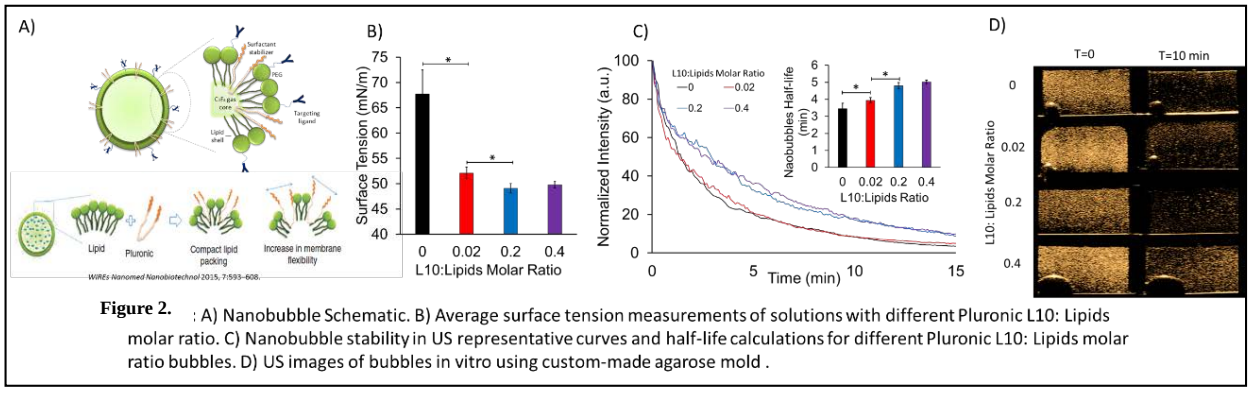


Figure 2. : A) Nanobubble Schematic. B) Average surface tension measurements of solutions with different Pluronic L10: Lipids molar ratio. C) Nanobubble stability in US representative curves and half-life calculations for different Pluronic L10: Lipids molar ratio bubbles. D) US images of bubbles in vitro using custom-made agarose mold .

1.3. On the Fate of Mesh-stabilized Lipid Nanobubbles after Destruction with Ultrasound

The dissipation of ultrasound signal from microbubble contrast agents has been linked to their fragmentation, jetting or sonic cracking, leading to a loss of gas. With strong interest in the use of bubbles in vivo, their ultimate fate is of great importance. It has been hypothesized that remnant shells shed into the surround aqueous medium, folding into liposomes or micelles. To investigate these effects, we have applied cryogenic transmission electron microscopy (cryo-EM) to image nanoscale lipid and polymer-stabilized perfluorocarbon gas bubbles before and after their destruction with high intensity US.

Methods: Polymer-stabilized lipid nanobubbles (NBs) were made by agitation of a lipid solution(DPPC:DPPE:DPPA), Pluronic L10, acrylamide monomers, crosslinker and irgacure 2959 in the presence of C_3F_8 gas, followed by crosslinking under U.V. light. Bubbles were imaged in an agarose mold in PBS using contrast harmonic imaging (Toshiba, 12 MHz, MI 0.1). Flash/replenish (20 cycles) was used to destroy bubbles. Particle size was determined by dynamic light scattering. For cryo-EM, NBs were applied to EM grids (R2/2, 400 mesh; EMS) glow-discharged for 30 sec at 15 mA and imaged on JEOL 2200FS transmission electron microscope with a total electron dose of <100 e^-/A^2.

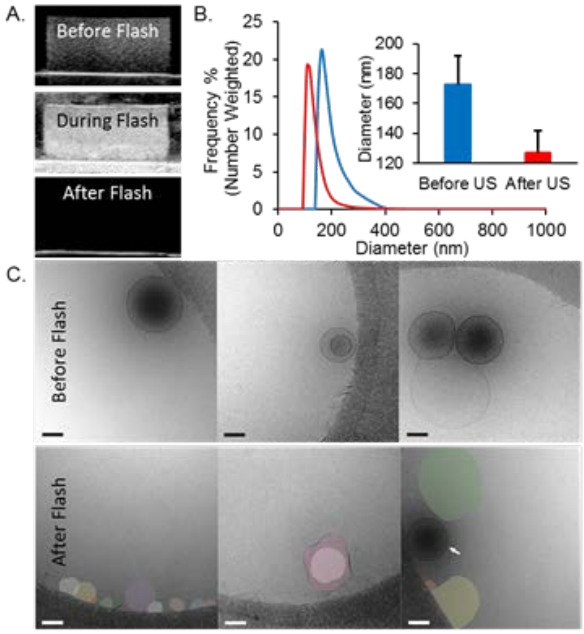


Figure 3. Change in nanobubble (A) US signal, (B) size and (C) shape (by cryo-EM) before and after destruction with high intensity US. Color added to cryoEM images for better visualization. Scale bars represent 100nm.

Results and Discussion: The application of the high intensity US was found to destroy all bubble contrast (**Fig 3a**). Mean NB diameter was significantly reduced from 172.7 ± 19.3 nm to 126.7 ± 15.0 nm suggesting a loss of gas from the particles (**Fig 3b**). Cryo-EM images of NBs demonstrate that particles have a monolayer shell with a dark center that is likely due to the higher density of the frozen C_3F_8 core relative to the surrounding water layer. Sonicated NBs appeared as amorphous and transparent lipid sheets, indicating a loss of gas (**Fig 3c**). While some multi-laminar vesicles were present in the NB solution prior to sonication, none could be visualized in the US disrupted solution. These results suggest that US-disrupted NBs do not reform as liposomes or micelles but rather flatten into round sheets following gas loss. This unexpected result may be due to the hydrophobic acrylamide core helping to maintain particle structure.

1.4. Ultrasound Signal from Sub-Micron Lipid-coated Bubbles

It remains unclear whether nanoscale lipid-stabilized bubbles can produce the observed enhanced acoustic backscatter at clinically relevant frequencies. Because NB polydispersity is high, micron sized bubbles are thought to contribute to experimental observations. Accordingly, this study examined echogenicity of lipid- and surfactant-stabilized perfluoropropane (C_3F_8) nanobubbles (NBs), rigorously controlling for the presence of microbubbles in the solution.

Methods**:** NBs were formulated by mechanical agitation of a PBS solution of lipids (DBPC:DPPE:DPPA), Pluronic L10, and glycerol in the presence of C_3F_8 gas. Microbubbles were separated from NBs based on their buoyancy by centrifugation. According to the Stokes equation (**Fig 4A**), when centrifuged at 50g for 5 min a bubble larger than 0.7 um should rise a distance of 0.5 cm. Care was taken to only collect samples below this distance. Particle size and buoyant mass were measured using Resonant Mass Measurement (RMM), Archimedes, Malvern Instruments). Isolated NBs were filtered using track-etched polycarbonate filters of 1000 nm and 400 nm using

a syringe pump at 0.125 mL/min and 0.5 mL/min and were imaged in an agarose mold in PBS using contrast harmonic imaging (Toshiba, 12 MHz, MI 0.1).

Results and Discussion: RMM results (**Fig. 4B**) show that mean NB size was 469 nm and all buoyant particles (negative mass) were below 1 µm. These large positive mass particles are likely large lipid aggregates and should not produce ultrasound signal. US images of isolated NBs (**Fig. 4C**) demonstrate considerable echogenicity. A reduction in signal after filtration was noted (**Fig 4C**), but NB activity was observed under all conditions. It is not clear whether the signal decrease is due to lower NB concentration or smaller bubble size. It is likely that filter pore blockage by lipid aggregates is responsible for some of the signal loss. Figure 4E shows microscopy and Nanosight particle size distribution following centrifugation. No particles larger than 700 nm were seen. While the mechanism of the strong NB activity at 12 MHz is not fully understood, a reduction of surface tension by the surfactant Pluronic, or buckling of the shell in response the US field, are likely contributors.

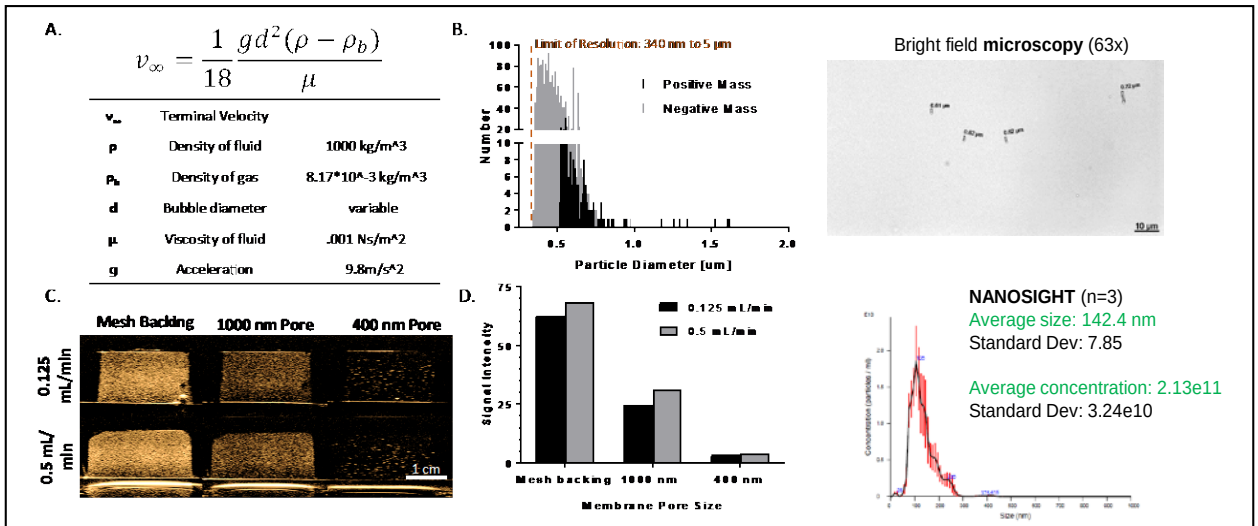


Figure 4. (A) Stokes law for the terminal velocity of a bubble. (B) Particle size distribution based on buoyancy determined by RMM with a lower limit of detection at 340 nm. US images (C) and corresponding grayscale intensity (D) of isolated NBs before and after being filtered through 1000 nm and 400 nm pores. (E) Microscopy and particle size analysis following centrifugation.

1.5. Characterization of PSMA-1-cys peptide synthesis and lipid conjugation via MALDI-TOF and Ellman's analysis

The lipids (DSPE-PEG, DSPE-PEG-MAL and L-cysteine were dissolved in 0.1M phosphate buffer. L-cysteine was added to the DSPE-PE and DSPE-PEG-MAL groups and the samples were evaluated for thiol content using Ellman's assay. Two different MAL:Thiol ratios were used (2:1 and 2:0.5). It is evident from **Fig. 5A**, that the reaction takes place rapidly, and no change is seen after 10 minutes. The level of thiol groups in the 2:0.5 ratio group decreased to control levels

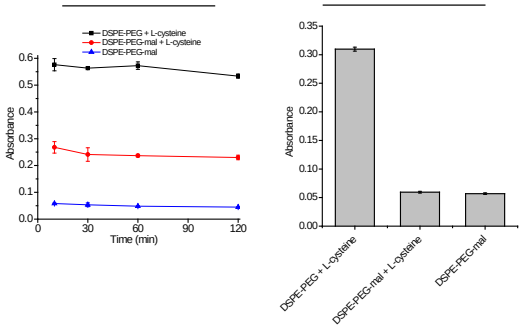
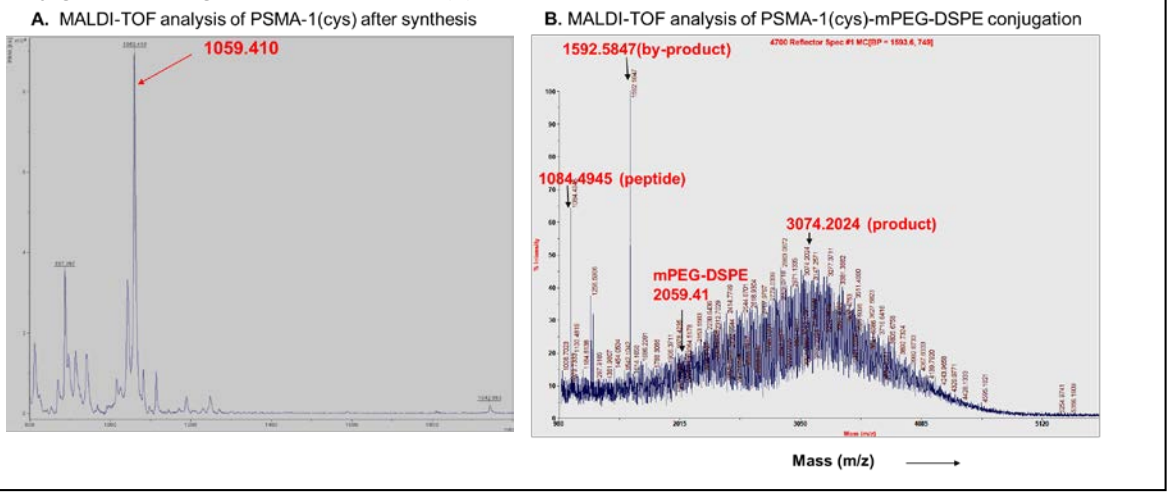


Figure 5. Confirming efficiency of lipid-mal-cys

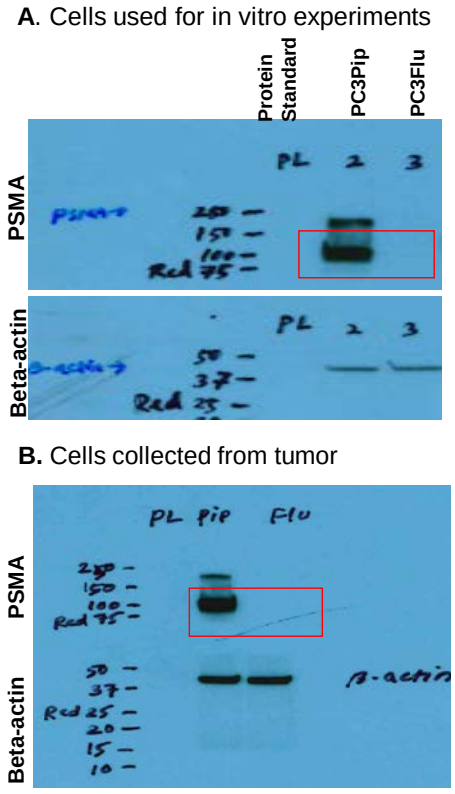
after 10 min (**Fig. 5B**), indicating near complete binding of cysteine to the DSPE-PEG-MAL group. Characterization of PSMA-1-cys peptide synthesis and lipid conjugation to PSMA-1-cys was confirmed by Matrix Assisted Laser Desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) analysis. The results are shown in **Fig 6A-B**.

Figure 6. MALID-TOF analysis confirming the successful synthesis of PSMA-1-cys ligand (**A**) and of the successful conjugation of the ligand to DSPE-PEG-Mal (**B**).



1.6. Confirmation of PSMA biomaker expression in cell lines via Western blotting

Figure 7. Confirmation of PSMA expression in cells (**A**) and tumors (**B**)



Methods: PC3pip (PSMA positive) and PC3Flu (PSMA negative) cells were grown to the logarithmic phase, rinsed with phosphate-buffered saline (PBS), placed on ice, and suspended in 200 µl of radioimmunoprecipitation assay (RIPA) protein lysis buffer. Next, all cells/tumor lysates were transferred to a 1.5-mL tube and centrifuged at 12000 rpm and 4°C for 15 min. The resulting supernatant was transferred to a new 1.5 mL centrifuge tube. A bicinchoninic acid (BCA) kit was then used to determine the protein concentration. Additionally, the samples were supplemented with 2X Laemmli loading buffer, mixed and boiled for 5 min to fully denature the proteins. Twenty micrograms of total protein was separated via SDS-PAGE and transferred to a nitrocellulose membrane via the semi-dry blotting method. Membranes were blocked with 5% milk in Tris Buffered Saline-Tween 20 (TBST) for 1 hour at room temperature. PSMA was detected with mAb J591 0.2 mg/mL for 1 hour followed by incubation with horseradish peroxidase-goat–anti-mouse IgG antibody (1:5,000 dilution) for 1 hour. After 3 TBST washes, blots were visualized by chemiluminescence. **Fig 7** confimrs expression of PSMA in both the PC3pip cell line as well as tumors grown from PC3pip cells. Lack of expression is seen in the PC3flu lines in both experiments.

Competition Binding Assay

Methods: Cells ($5X10^5$) were incubated with free PSMA-cys/ PSMA-1-NB and N-[N-[(S)-1,3-dicarboxypropyl]carbamoyl]-S-[3H]-methyl-L-cysteine (3H-ZJ24; GE Healthcare Life Sciences) in a total volume of 200 mL of 50 mmol/L Tris (pH 7.5) for 1 hour at 37 deg C. The mixture was centrifuged at 3,000 g for 5 minutes at 4 deg C to separate bound and free 3H-ZJ24. The supernatant was removed, and the cell pellet was washed 3 times with 500 mL of cold Tris buffer. Four milliliters of ECOLUME scintillation cocktail (MP Biomedicals) was added, and radioactivity was counted. Data were analyzed using GraphPad Prism 3.0.

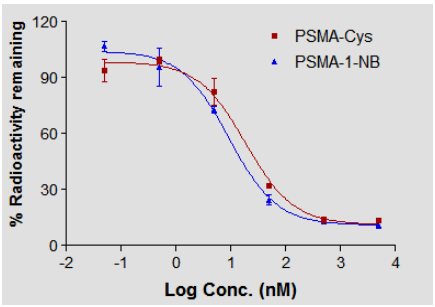
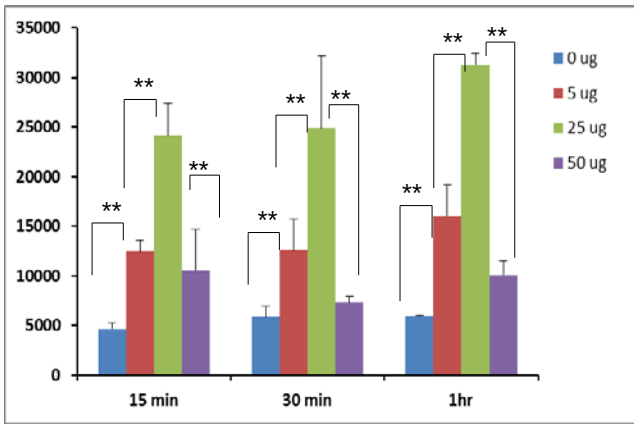


Figure 8. Competitive binding assay of PSMA-1 conjugated NBs where NB1 and NB2 constituted different methods of formulation of bubbles. IC50 values for PSMA-Cys and PSMA-1-NB were 18.6 nM and 9.2 nM

Results: Results show that the IC50 of PSMA-1- NB is lower (9.2 nM) than the ligand PSMA-1 (18.6 nM) (**Fig. 8**) in PSMA positive LNCaP cells.

1.7. In vitro binding studies (optimization of ligand density and cell microscopy)

Methods: Lipid conjugation of PSMA-Cys was performed through the -SH group of cysteine. PSMA-Cys was dissolved in anhydrous DMSO, to which 2.5-fold excess amount of Maleimide-PEG(2k)-DSPE was added. To formulate NBs, lipids DPPC, DPPE, DPPA and DSPE-PEG-PSMA-1 were dissolved in chloroform at a 4:1:1:1 ratio, dried and hydrated in PBS with Pluronic L10 solution. For optimization of binding, 40,000 cell/well were seeded 24 hr. before experiments. Bubbles with varying amounts of PSMA-cys ligand (0, 5, 25 and 50 ug (by weight)) were added and incubated for 15, 30 and 60 min. Rhodamine-DSPE was used to label to NBs. Cells were then washed with PBS and fluorescence per well analyzed with a plate reader.



*Statistical analysis is done by student's t-test where **P<0.01*

Figure 9. Binding optimization of PSMA-1-NBs (fluorescence from rhodamine-DSPE) in PC3pip cells. Data were obtained from fluorescence plate reader analysis.

For microscopy studies, 800,000 cells were seeded in 35 mm dish 24 hr before the experiment. Each dish contained one glass cover slip. On the day of experiment cells were washed by PBS for at least 2 times. Then the cells were incubated at 37 deg C either with unmodified or modified NBs for an hour. Cells were washed 2 times with PBS after incubation and fixed with 4% paraformaldehyde for 10 min. The cover slips were transferred to new dish and washed again for 3 times with PBS.

Finally cell nucleus was tagged with DAPI and slides were prepared with the cover slips. Image was taken with LEICA fluorescence microscope 25X.

Results: NBs were fluorescently tagged by adding rhodamine-DSPE into the lipid film. As evident in **Fig. 9**, nanobubbles containing 25 ug of PSMA-cys are better in targeting than other formulations. To determine cell binding, PSMA-expressing cells (PC3pip) and cells that do not express PSMA (PC3flu) were seeded ($1x10^6$ cells) onto 35mm dishes containing a cover slip 24 hrs prior to the experiment. Incubation of NBs with cells in culture for 60 min showed that targeted NBs accumulated significantly higher in PC3pip cells (**Fig. 10**). Data were collected using a fluorescent microscope and images processed to quantify fluorescence signal in cells. These preliminary *in vitro* data suggest that these PSMA-1 functionalized NBs indeed are able to bind cells expressing PSMA biomarker.

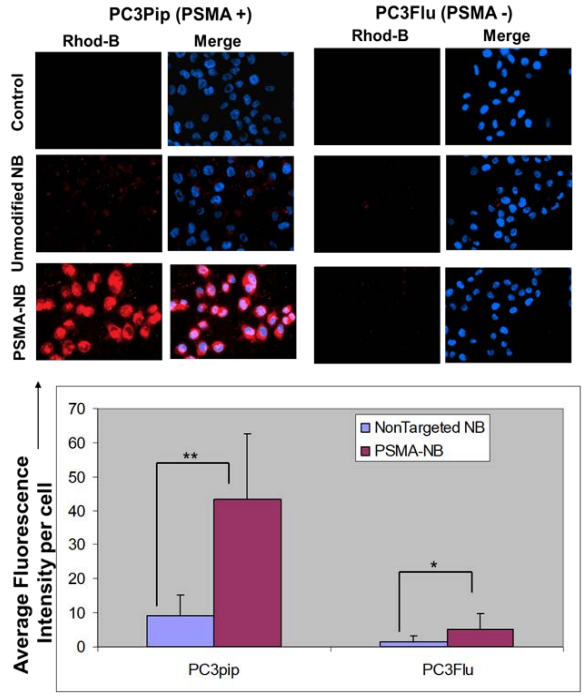


Figure 10. Binding of PSMA-1-NBs (fluorescence from rhodamine-DSPE) in PC3pip and PC3flu cells (A) and the respective quantification of microscopy data (B).

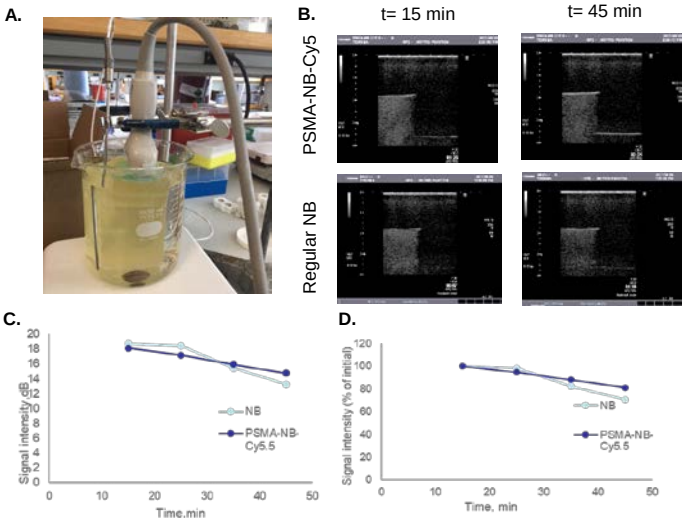


Figure 11. Acoustic characterization of NBs in phantom setup (A). Images were acquired with clinical ultrasound (B). Experiments compared the signal intensity (C) and signal decay (D) for PMSA and cy5.5 functionalized and non-functionalized nanobubbles. No differences were seen between groups.

1.8. Acoustic characterization of PSMA-1-NB

Following conjugation of the PSMA-1-cys ligand to DSPE-PEG-MAL lipid, we formulated nanobubbles using standard procedures. Initially, we did not stabilize these with polymers, because we wanted to explore the simpler bubble formulation strategy. Nanobubbles were then assessed via ultrasound imaging for their initial signal intensity as well as signal decay over time.

Methods: These experiments were conducted at physiological temperature, in a stirred system depicted in **Fig 11**. Bubbles were diluted into the PBS bath, and US

images were acquired at 1 frame every 10 seconds for the first 5 min, followed by periodic imaging for 30 minutes. A 12 MHz contrast harmonic imaging protocol was used, as described above. The decay and initial signal of functionalized nanobubbles also labeled with Cy5.5 fluorescent probe to that of standard, non-functionalized nanobubbles, to determine whether the surface decoration de-stabilized the bubbles or lead to a reduction in echogenicity.

Results: Both bubble types showed good stability over time and a 20% signal decay over 45 minutes. There was no difference seen with functionalized bubbles. This suggests that the addition of PSMA-1 ligand and the fluorescent label do not alter the signal intensity or the stability of the nanobubbles.

2. Overview of research accomplished pertaining to Task 2

The IACUC protocol has been approved, and we have begun to carry out initial in vivo experiments. Initial testing focused on establishing the appropriate tumor model geometry (location of the biomarker positive and negative tumors), and determining the PSMA-1 binding/uptake in both tumor types via optical imaging. In addition, we carried out ultrasound experiments comparing the kinetics of nanobubbles to that of commercially available microbubbles. These experiments serve to determine whether non-functionalized nanobubbles behave differently in the PC3 tumors then larger bubbles.

2.1. Confirming PSMA expression in vivo

Tumors were Mouse tumor xenograft models: All animal procedures were performed according to Institutional Animal Care and Use Committee (IACUA)-approved protocols. For flank tumor xenografts, 6- to 8-week-old athymic nude mice were implanted subcutaneously with 1×10^6 of PSMA-negative PC3flu and PSMA-positive PC3pip cells in 75 µL Matrigel on the right leg. Animals were observed every other day until tumors reached at about 5-6 mm in diameter. After 2 weeks, animals were ready for experiment.

In vivo imaging studies: Imaging was performed with the aid of the Maestro Imaging System (Perkin-Elmer) with each mouse receiving 1 nmol of NIR probe in PBS through tail vein injection. Imaging was performed at different time points using the appropriate filter set (deep red filter set for PSMA-1–IR800). During imaging, the temperature of imaging bed was adjusted to 37°C. Mice received inhalation of isofluorane through a nose cone attached to the imaging bed. Mice were imaged over 24 hr post injection.

Results are shown in **Fig 12.** The PSMA-1-IR800 can be seen accumulating in the Pc3pip tumors but not in the Pc3flu tumors. The peak accumulation was at 2.5 hours following injection. This experiment confirmed that the tumors express the biomarker and can be imaged with optical imaging. Next steps include repeating these experiments with fluorescent PSMA-1-NBs. These studies are currently in the planning stages and will commence later this year.

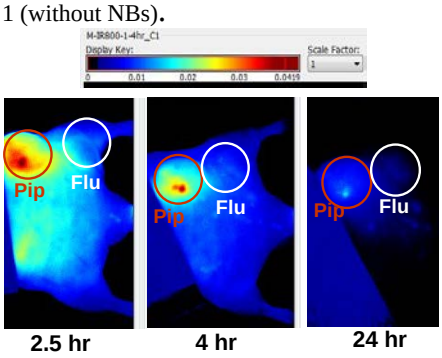


Figure 12. Optical imaging of PC3pip and PC3flu tumors grown adjacent to each other in mouse flank. Images were acquired following IV injection of fluorescent PSMA-1 (without NBs).

2.2. Nanobubbles Enhance Ultrasound Imaging of Prostate Tumors in Mice

The most widely used ultrasound contrast agents are lipid or protein-stabilized perfluorocarbon (PFC) gas microbubbles (MB) typically exceeding 2µm in diameter. These bubbles usually show rapid transient tumor enhancement, as they are confined to vasculature. To achieve longer lasting enhancement and improved delineation of tumors, we developed sub-micron lipid and surfactant-stabilized PFC nanobubbles (NB). Here we compared tumor kinetics of the NBs compared to commercially available MBs.

Methods: C_3F_8 NBs were formulated by dissolving a cocktail of lipids including DBPC, DSPE-PEG in PBS followed by gas exchange and activation via mechanical agitation. NBs were purified by centrifugation, and size was measured by dynamic light scattering (DLS). Tumors were inoculated in the flank of three male nude mice by injection of PC3 prostate cancer cells in Matrigel®, and grown to 5-8 mm (**Fig. 13A**). Contrast-enhanced US images were acquired with Vevo 3100 (Visualsonics Fujifilm) at 1fps, 18MHz, and 4% power following tail vein injections of 100 ul of either MicroMarker (Visualsonics) or NBs. Maximum intensity projection (MIP) and time-intensity curves (TIC) were obtained in the same mouse for both contrast agents.

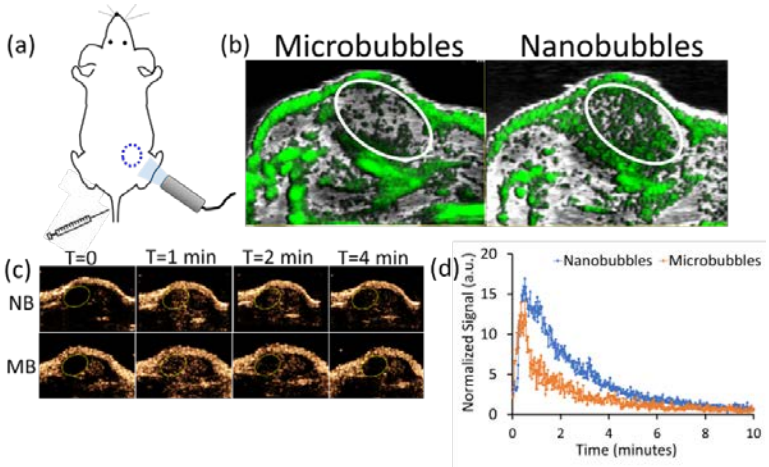


Figure 13: (a) Schematic of animal tumor model and US scan orientation. (b) MIP comparison in PC3 flank tumor 15s after contrast injection. (c) Representative tumor images of NBs and MBs from the same mouse. (d) Mean TIC curves for NBs and MBs.

Results/Discussion: NBs have a diameter of 240±95 nm, (compared to 2-3µm for MicroMarker). MIP images (**Fig. 13B**) show that NB provided more signal throughout the tumor cross section compared to MBs at t=15s. Representative contrast images are shown in **Fig. 13C** and the mean TIC for all replicates is shown in **Fig. 13D.** NBs had a half-life of 2.1min compared to 1min for microbubbles, and at t=2 min showed a signal intensity nearly 3 times higher than MBs. Higher tumor signal and slower wash out suggests that smaller NBs were able to penetrate out of the leaky tumor vasculature and further into the tumor interstitium. Such NBs may eventually provide a more effective contrast agent compared to MBs and could enhance US guided biopsies.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

We hired two postdoctoral fellows, Drs. Jacob Liliy and Afsana Akhter as part of this project. This was the first postdoctoral training experience for both individuals, and they have obtained advanced professional skills training via various interactions with mentors, attended seminars, supervised graduate and supervised undergraduate students.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report." Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

We are currently mentoring two high school students from local Cleveland schools in the laboratory. They have exposure to all of the projects in our laboratory including this one.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

As Tasks 1-2 summarize, in the next reporting period, we plan to continue carrying out NB formulation optimization to further reduce the size, increase stability of ultrasound signal and maximize cell binding and uptake in vitro. We also plan to carry out many more of the in vivo tests in mouse models to examine the biodistribution of fluorescent NBs conjugated to PSMA-1 compared to un-targeted NBs in PSMA+ and PSMA- tumors with optical imaging and ultrasound.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Currently, we are only 30% into the project, and we have not yet had the opportunity to determine the broader impact of this research on our discipline or other disciplines. In general, we are intending to broaden the scope of ultrasound imaging applications that can have true patient impact. This includes developing additional molecular imaging applications, and better nanobubble formulations. We are also working to better understand the fundamental biophysical and acoustical reasons behind the unique NB behavior. This will take some additional time.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. **CHANGES/PROBLEMS:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

We had initial issues with the (PC3pip) cells which express and do not express (PC3flu) PSMA biomarker being cross-contaminated. Steps were immediately taken to resolve the issues, and, as seen in the biomarker expression results, we have now resolved the contamination issues. We do not expect additional problems to arise, but will test PSMA expression in our cell lines periodically to confirm.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Hernandez C, Gulati S, Stewart P, Exner AA. Cryo-EM Visualization of Lipid and Polymer-Stabilized Perfluorocarbon Gas Nanobubbles. Scientific Reports. In preparation.

  Nieves L, Exner AA. Effect of the Surfactant Pluronic on the Stability of Lipid-Stabilized Perfluorocarbon Nanobubbles. IEEE International Ultrasonics Symposium 2017 Proceedings. *In preparation.*

  Hernandez C Exner AA. Ultrasound Signal from Sub-Micron Lipid-coated Bubbles. IEEE International Ultrasonics Symposium 2017 Proceedings. *In preparation.*

  Hernandez C, Gulati S, Stewart P, Exner AA. On the Fate of Mesh-stabilized Lipid Nanobubbles after Destruction with Ultrasound. IEEE International Ultrasonics Symposium 2017 Proceedings. *In preparation.*

  Lilly J, Xia H, Ankher A, Ramamamurthy G, Basilion J, Exner AA. Nanobubble Contrast Agents Enhance Ultrasound Imaging of Prostate Tumors in Mice. IEEE International Ultrasonics Symposium 2017 Proceedings. *In preparation.*

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to report.

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

1. Afsana Akhter, Jacob Lilly, Christopher Hernandez, Gopalkrishnan Ramamurthy, Hansheng Xia, Xinning Wang, Agata A. Exner, James P. Basilion. In vitro assessment of a novel PSMA-targeted nanobubble for prostate cancer ultrasound imaging. World Molecular Imaging Congress. 2017. *Under review.*
2. C Hernandez, L Nieves, J Lilly, H Xia, A Ankher, X Wang, G Ramamurthy, R Advincula, J Basilion, MC Kolios, AA Exner. Toward successful ultrasound molecular imaging of cancer with nanobubble contrast agents. Contrast Media Research 2017. *Under review.*
3. Gabriella Fioravanti, Christopher Hernandez, Agata A. Exner. Lipid Acyl Chain Length Improves Stability of Nano-sized Ultrasound Contrast Agents In Vitro. Biomedical Engineering Society 2017 meeting. Under review.
4. Nieves L, Exner AA. Effect of the Surfactant Pluronic on the Stability of Lipid-Stabilized Perfluorocarbon Nanobubbles. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*
5. Hernandez C Exner AA. Ultrasound Signal from Sub-Micron Lipid-coated Bubbles. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*
6. Hernandez C, Gulati S, Stewart P, Exner AA. On the Fate of Mesh-stabilized Lipid Nanobubbles after Destruction with Ultrasound. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*
7. Lilly J, Xia H, Ankher A, Ramamamurthy G, Basilion J, Exner AA. Nanobubble Contrast Agents Enhance Ultrasound Imaging of Prostate Tumors in Mice. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Oral presenation.*
8. Nieves L, Hernandez C, Exner AA. Structure-Function Relationship between Lipid Shell Components and Surface Tension of Nanobubble Ultrasound Contrast Agents; 2016 Annual Biomedical Research Conference for Minority Students (ABRCMS) Tampa, FL; *Poster Presentation*
9. Nieves L, Hernandez C, Exner AA. Structure-Function Relationship between Lipid Shell Components and Surface Tension of Nanobubble Ultrasound Contrast Agents; SFB Midwest 2016, *Oral presentation;* *Honorable Mention Award*
10. Fioravanti G, Hernandez C, Exner AA, Lipid Acyl Chain Length Improves Nanosized Contrast Agents Stability In Vitro; SFB Midwest 2016, *Oral presentation*
11. Hernandez C, Wang X, Basilion J, Exner AA. Early Detection of Prostate Cancer with New Nanoparticle-Based Ultrasound Contrast Agents Targeted to PSMA. 2016 World Molecular Imaging Conference. *Poster presentation.*

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Invention #: 2017-3125 Title: PSMA Targeted Nanobubbles for Diagnostic and Therapeutic Applications Patent filing: Provisional patent, 62/381,144 Filing date: August 30, 2016 Funding reported: DoD W81XWH-16-1-0371 Summary: This application relates to diagnostic and therapeutic compositions, and more particularly to targeted nanobubbles for diagnostic, therapeutic, and theranostic applications. Abstract: A PSMA targeted nanobubble includes a membrane that defines at least one internal void, which includes at least one gas, the membrane including at least one lipid, at least one nonionic triblock copolymer that is effective to control the size of the nanobubble without compromising in vitro and in vivo echogenicity of the nanobubble, and an interpenetrating cross-linking biodegradable polymer; and at least one PSMA ligand coupled or linked to the membrane.

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

<u>Example:</u>

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name:	Agata Exner PhD
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	AEXNER (NIH Commons)
Nearest person month worked:	2.4
Contribution to Project:	Oversees project operations
Funding Support:	Current grant and NIH R01EB016960
Name:	James Basilion PhD
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	JBASILION (NIH Commons)
Nearest person month worked:	1.4
Contribution to Project:	Oversees project operations
Funding Support:	Current grant and NIH
Name:	Jacob Lilly PhD
Project Role:	Postdoctoral fellow
Researcher Identifier (e.g. ORCID ID):	Not available
Nearest person month worked:	11
Contribution to Project:	Performed tasks pertinent to nanobubble formulation optimization and functionalization
Funding Support:	Current grant
Name:	Afsana Akhter PhD
Project Role:	Postdoctoral fellow
Researcher Identifier (e.g. ORCID ID):	Not available
Nearest person month worked:	11
Contribution to Project:	Performed tasks pertinent to PSMA ligand synthesis, conjugation, expression in cells, and in vivo models.
Funding Support:	Current grant
Name:	Xinning Wang
Project Role:	co-investigator
Researcher Identifier (NIH commons or ORCID ID):	Xining.wang (NIH Commons)
Nearest person month worked:	6 months
Contribution to Project:	synthesizing and purification of PSMA-1-Cys ligand; teaching the new postdoctoral how to make the peptide; Establish HPLC method to follow the reaction of PSMA-cys with DSPE maleimide; MALDI confirmation of the

	conjugation of PSMA-cys with the lipid; performing competition binding experiments for the ligands and nanobubbles, providing PSMA-1-IR800 for in vivo imaging experiments.
Funding Support:	this funding and RO1EB020353, RO1, NIHNIBIB

Name:	Lenitza Nieves
Project Role:	Lab technician
Researcher Identifier (e.g. ORCID ID):	Not available
Nearest person month worked:	7
Contribution to Project:	Carried out fundamental biophysical experiments to determine the bubble shell properties.
Funding Support:	CWRU NIH PREP program R25GM075207
Name:	Chris Hernandez
Project Role:	Graduate student
Researcher Identifier (e.g. ORCID ID):	CHRISTOPHER.HERNANDEZ
Nearest person month worked:	1.5
Contribution to Project:	Basic acoustic characterization and optimization of the nanobubbles
Funding Support:	F31 CA200373-01
Name:	Hansheng Xia
Project Role:	Visiting research fellow
Researcher Identifier (e.g. ORCID ID):	Not available
Nearest person month worked:	5
Contribution to Project:	Carried out ultrasound scans on agents in vitro and in vivo. Assisted with experiments
Funding Support:	Self-funded from China.

Name:	Gabby Fioravanti
Project Role:	Undergraduate researcher
Researcher Identifier (e.g. ORCID ID):	Not available
Nearest person month worked:	4
Contribution to Project:	Carried out experiments to determined shell property effects on bubble stability
Funding Support:	Pilot grant from Case Comprehensive Cancer Center P30CA043703 R01EB016960

H**as there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Exner: MPI on Mary Kay Foundation (MPI with Brady-Kalnay, DiFeo)
PTPmu as a targeting agent for ultrasound-mediated deployment and treatment of ovarian cancer. 7/1/2017-6/30/2019

Basilion: Nothing to report.

Ponsky: Co-investigator on 1R01CA208236-01A1; Project Start Date: 2-MAR-2017
Contact PI / Project Leader: GULANI, VIKAS
Title: MR FINGERPRINTING AND COMPUTERIZED DECISION SUPPORT FOR PROSTATE CANCER

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc.,*

available to project staff);

- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

I have included my CV.

AGATA A. EXNER, PH.D.

CURRENT APPOINTMENT

Professor
Department of Radiology
Case Western Reserve University School of Medicine
11100 Euclid Avenue, Wearn 353
Cleveland, Ohio 44106-5056
Phone: (216) 844-3544
Fax: (216) 844-5922
E-mail: **agata.exner@case.edu**

ACADEMIC APPOINTMENTS

2015-	Professor, Dept. of Radiology and Biomedical Engineering, Case Western Reserve University (CWRU), Cleveland, OH
2010-2015	Associate Professor (with tenure), Dept. of Radiology, CWRU
2010-	Associate Professor (secondary), Dept. of Biomedical Engineering, CWRU
2004-	Assistant Professor (secondary), Dept. of Biomedical Engineering, CWRU
2004-	Member, Case Comprehensive Cancer Center, Case Western Reserve University
7/2003-	Assistant Professor (primary), Dept. of Radiology, CWRU
2/2003-7/2003	Visiting Professor, Dept. of Radiology, CWRU
1998-2003	Graduate Research Associate, Dept. of Biomedical Engineering, CCWRU
1997-1998	Research assistant, Department of Biomedical Engineering, The Cleveland Clinic Foundation, Cleveland, OH
1996	Research assistant, Department of Macromolecular Science, CWRU

EDUCATION

2000-2003	**Ph.D.**, Biomedical Engineering Case Western Reserve University, Cleveland, OH Thesis title: Noninvasive CT Monitoring and Evaluation of Local Drug Delivery in Livers Following Radiofrequency Ablation (RFA). Advisor: Jinming Gao, Ph.D. (now at UT Southwestern)
1998-2000	**M.S.**, Biomedical Engineering Case Western Reserve University, Cleveland, OH Concentration: drug delivery / biomaterials / imaging
1994-1998	**B.S**. (*Magna Cum Laude*), Biomedical Engineering Case Western Reserve University, Cleveland, OH Concentration: Biomaterials; Minor: chemistry

SOCIETY MEMBERSHIP

2005-	Controlled Release Society
2004-	Radiological Society of North America
2001-	Society for Biomaterials
2004-06	American Association of Pharmaceutical Scientists
2010-11	Society for Molecular Imaging
2013-	Biomedical Engineering Society

HONORS

2015	Mather Spotlight Woman of Achievement Award, CWRU Flora Stone Mather Center
2015	Elected **Fellow of the American Institute of Medical and Biological Engineering (AIMBE)**
2014	Mentoring Award, CWRU Postbaccalaureate Research Education Program
2013-	Associate Editor for Annals of Biomedical Engineering
2013	Elected **Academy of Radiology Research Distinguished Investigator**
2011	Nominee for Graduate Student Mentorship Award, Dept. Biomedical Engineering
2011	Nominee for Northeast Ohio Athena Young Professional Award
2008	Radiology Research Fellow Prize at the Radiological Society of North America 2008 meeting (H. Wu et al)
2008	Nominee for Jackson Award for Excellence in Undergraduate Mentoring, CWRU
2007	Radiology Research Fellow Prize at the Radiological Society of North America 2007 meeting (H. Wu et al)
2007	Cum Laude Award for outstanding scientific paper, Society of Computed Body Tomography and Magnetic Resonance (S. Nour et al)
2006	Nominee for the Carl Wittke Award for Excellence in Undergraduate Teaching
2005	Learning Scholar, University Center for Innovation and Teaching Excellence
2004-2006	National Institutes of Health Clinical Research Loan Repayment Program Award
2002	Society for Biomaterials Travel and Professional Development Award
2002	New Jersey Biomaterials Symposium Travel Award
2001-2003	National Institutes of Health Trainee Research Grant
1998-2001	Whitaker Foundation Trainee Research Grant
1997-1998	Case Alumni Association Scholarship

PROFESSIONAL ACTIVITIES

2011-2017	Chartered member: Biomaterials and Biointerfaces (BMBI) Study Section, NIH
2017	Reviewer P20 COBRE proposals, NIBIB
2016	Reviewer for Florida Department of Health Zika Grant Program
2016	RTB Study section, NIH
2016	ZRG1 SBIB-Z (58) R Image Guided Drug Delivery SEP grant reviewer (NIH)
2015	Reviewer for Pennsylvania Department of Health (PA DOH) Oak Ridge Associated Universities Grant Program
2015	ZRG1 SBIB-Z (58) R Image Guided Drug Delivery SEP grant reviewer (NIH)
2014	Department of Defense CDMRP Prostate Cancer Research Program Scientific Reviewer
2014	Reviewer for Pennsylvania Department of Health (PA DOH) Oak Ridge Associated Universities Grant Program
2014	Mentor, Minority Access to Research Careers (MARC) program, Emory University
2014	2014/05 ZCA1 SRLB-J (M1) S Quantitative Imaging for Evaluation of Responses to Cancer Therapies- U01 grant mail reviewer
2014	2014/05 ZRG1 SBIB-Z (58) R Image Guided Drug Delivery SEP grant reviewer (NIH)
2014	Society for Biomaterials, Session Organizer and co-Chair
2013	Department of Defense peer review panel of the 2013 Peer Review Medical Research Program (PRMRP)
2013	Reviewer for Pennsylvania Department of Health (PA DOH) Oak Ridge Associated Universities Grant Program
2013	ZRG1 SBIB-J (57) R Academic-Industrial Partnership Scientific Reviewer
2013	Department of Defense CDMRP Prostate Cancer Research Program - Online Reviewer
2012	Grant reviewer for Pennsylvania Department of Health (PA DOH). Oak Ridge Associated

	Universities
2012	ZRG1 SBIB-Q 04 member conflict review study section ad hoc reviewer
2012	PCRP Preapplication-Cell Biology-1 - Online Reviewer
2012	PCRP Preapplication-Clinical and Experimental Therapeutics-2 - Online Reviewer
2012	Society for Biomaterials abstract reviewer for 2012 Fall Symposium
2011	Department of Defense CDMRP Prostate Cancer Research Program Scientific Reviewer
2011-	Member, IACUC Committee on Electronic Protocol Submission and Review
2011-	Co-Chair, Cancer Imaging Program group on Image-guided drug delivery (Case Comprehensive Cancer Center)
2011-	Co-Chair, Pilot Funding Initiative for Image Guided Biomaterials Development (Institute for Advanced Materials and Case Center for Imaging Research)
2011	Centers of Biomedical Research Excellence ad hoc reviewer (NCRR)
2011	Session Chair (Cancer Drug Delivery) Society for Biomaterials 2011 Meeting
2011	Grant reviewer for Pennsylvania Department of Health (PA DOH). Oak Ridge Associated Universities
2010	Grant reviewer for the Council for Chemical Sciences (CW) of the Netherlands Organization for Scientific Research (NOW)
2010	Cleveland Science Café presenter
2010	Department of Defense CDMRP Prostate Cancer Research Program Scientific Reviewer
2010	NIH Study Section Ad hoc, Biomaterials and Biointerfaces – BMBI, Radiation Therapeutics and Biology- RTB, ZRG1 OTC-K Cancer Therapeutics
2010	Science Fair judge for Hathaway Brown School
2009	Peer review panel member (Ad hoc Clinical and Experimental Therapeutics 2009 Prostate Cancer Research Program for DoD Congressionally Directed Medical Research Programs)
2009-10	Society for Biomaterials Symposium Co-Chair for 2010 meeting “Micron and Nanotechnology Derived Theranostic Biomaterials”
2009-	*Therapeutic Delivery* journal Editorial Advisory Board member
2009	NIH Study Section (Ad hoc, Special emphasis panel, Ruth L. Kirschstein National Research Service Awards, BMBI)
2009	NIH ARRA Challenge Grant reviewer (3 panels)
2008-10	Guest Co-Editor *Molecular Pharmaceutics* Special issue on image-guided drug delivery
2009	Science Fair judge for Hathaway Brown School
2009-	Research mentor for Hathaway Brown School Research Program
2008	Abstract Reviewer, Society for Biomaterials Annual Meeting 2009
2008	NIH Study Section (Surgical Sciences, Biomedical Imaging and Bioengineering, ad hoc)
2006	NIH Study Section (Gene and Drug Delivery, NCI, ad hoc: 2006, 2007)
2004	Invited participant, Image-Guided Interventions Workshop
2003-	*Active reviewer for the following journals:* Journal of Controlled Release, Pharmaceutical Research, Clinical Cancer Research, Experimental Biology and Medicine, Technology in Cancer Research and Treatment, Molecular Cancer Therapeutics, Annals of Biomedical Engineering, Journal of Pharmacy & Pharmaceutical Sciences , Journal of Pharmaceutical Science, Journal of Biomedical Materials Research
2003	Intel International Science and Engineering Fair – Judge

UNIVERSITY SERVICE

2017-	Associate Director, Medical Scientist (MD/PhD) Training Program (MSTP)
2017-	MSTP Steering Committee Member
2016-2017	Dept. of Macromolecular Science search committee member
2016-	Committee on Biomedical Research, Executive Committee, School of Medicine

2016-	Cancer Center Education Committee member
2016-	Institute for Advanced Materials V2.0 Planning Committee member
2015-	**Chair, Institutional Animal Care and Use Committee**
2014	IACUC Noncompliance Subcommittee Chair
2014	Committee on Research Misconduct Member
2014-	Interactive Commons @ CWRU Steering Committee member
2014-	Institute for Advanced Materials (IAM) @ CWRU Steering Committee member
2013-	Organizer and Chair- Case Center for Imaging Research Study Section, CWRU
2012-2015	Elected member, Committee on Budget, Finance, and Compensation-School of Medicine
2012-	CWRU Postbaccalaureate Research Education Program Research Mentor
2012-2013	Institutions Developing Excellence in Academic Leadership (IDEAL) Project Follow-up Committee Member
2012-	Women Faculty of the School of Medicine Steering Committee member
2012-2013	IACUC, Protocol Development Subcommittee Member
2012-	WISER Professional Mentoring Program Designated Mentor
2012	Department of Radiology /CCIR salary metrics committee chair
2012-	Cancer Imaging Program Image-Guided Drug Delivery Subcommittee Chair
2012	Member -- Search committee for Vice Dean of Faculty Development and Diversity, CWRU School of Medicine
2009-	Academic CCIR liaison to Radiology education office
2009	Academic Integrity Board Panel member, CWRU Orientation
2008-2011	Elected faculty rep for associate faculty of Department of Biomedical Engineering
2008-	CCIR Internal Grant Review Panel organizer and chair
2008-	Member – Institutional Animal Care and Use Committee
2008-	Member- Academic Integrity Board
2008-	Interviewer for the Pre-Professional Scholars Program, UG Admissions
2008-	Member - Postbaccalaureate Research Education Program Steering Committee
2008	Panel member BME Research Day Breakout Session: Career Paths after Graduation
2007-08	Faculty search committee member – Department of Biomedical Engineering
2007-09	Panel member – New Faculty Orientation (CWRU)
2007-	Senior mentor – CWRU Medical Sciences training Program
2006-07	Organizer – Frontiers in Biomedical Imaging seminar series
2006-2009	CWRU Medical School Admissions interviewer
2006	Thesis committee member - Department of Chemistry Honors program, Kenyon College
2006	Faculty - Student Forum panel member, UCITE and Office of Greek Life
2006-	Small Animal Imaging Research Center Advisory Committee – member
2005	Biomedical Engineering Research Day – Poster Judge
2005-2007	Junior mentor – CWRU Medical Sciences training Program
2004-	Member -- Case Comprehensive Cancer Center
2004, 2007-	Department of Radiology Committee on Appointments, Promotions and Tenure
2003-2004	Department of Radiology Construction & Renovation Committee Member
2003-2008	Case Western Reserve University Research Showcase – Poster Judge

TEACHING EXPERIENCE

Faculty / Research advisor – EBME 398 Senior Capstone Undergraduate Research | 2003- present
Guest lecturer faculty – EBME 105 Introduction to Biomedical Engineering | 2003- present
Faculty – EBME 328/329, Undergraduate Biomedical Laboratory 2010-present
Guest lecturer faculty – EBME 462 Cellular and Molecular Imaging | 2010-present
Faculty – EBME 319, Undergraduate Biomedical Laboratory | 2009
Guest lecturer and small group facilitator -- EMBE 316/416 2008-2010
Group advisor – EBME 380, Senior Design Project | 2005, 2007, 2008, 20015
Course co-design, faculty -- EBME 316/416, Biomaterials in Drug Delivery |2006-2008

Teaching assistant, guest lecturer – EBME 416, Biomolecular Engineering | 2000
Teaching assistant– EBME 408, Tissue Engineering | 1999

RESEARCH ADVISEES AND STAFF

POSTDOCTORAL

2017-	Al de Leon (*Postdoctoral Fellow)*
2016-	Afsana Ankher, Ph.D. (*Postdoctoral Fellow, co-mentored with Jim Basilion, CWRU)*
2016-	Jacob Lilly, Ph.D. (*Postdoctoral Fellow)*
2006-2014	Hanping Wu M.D., Ph.D. (*Senior Research Associate, departing June 2014 for residency*)
2007-08	Yuanyi Zheng, M.D., Ph.D. (*currently PI at Hospital of Chongqing Medical University*)
2010-11	Bryan Traughber, M.D. (*currently Philips Research Fellow at Seidman Cancer Hospital*)
2010-11	Tianyi Krupka, Ph.D. (*currently Postdoctoral fellow, Stanford University*)
2009-11	Luke Wilkins, M.D. (*currently Fellow at Medical University of South Carolina, Interventional Radiology*)
2010-2015	Reshani Perera, Ph.D. (*Senior Research Associate*)
2012-2013	Luis Solorio, Ph.D. (*Department of Defense Postdoctoral Fellowship Recipient, currently Assistant Professor, Dept. Of Biomedical Eng. Purdue University*)
2014	Tianzhi An, M.D., Ph.D. (*PI at research hospital in Beijing, China*)
2014-2015	Ravi Patel M.D., Ph.D. (*Resident at UH Case Medical Center, Radiation Oncology)*
2014-2015	Yong Gao (*Visiting PhD Scholar from Guangxi Medical University, China*)
2015-2016	Hai-Xia Yuan, M.D. (*Visiting Scholar from Zhongshan Hospital of Fudan University, Shanghai, China*)
2016-2017	Hansheng Xia, M.D. (*Visiting Scholar from Zhongshan Hospital of Fudan University, Shanghai, China*)

GRADUATE / MEDICAL

2004-07	Brent Weinberg (*MD/PhD, MSTP, currently Assistant Professor, Dept. of Radiology, Emory University*)
2004-05	Sonali Mehandru (*MED, Pediatric Radiologist, Children's Hospital of Colorado*)
2006-10	Ravi Patel (*MD/PhD, MSTP, Radiation Oncology Resident at CWRU, Going to U of Wisconsin, Madison*)
2006-10	Tianyi Krupka (*PhD, BME, completed postdoct at Stanford University, Co-Founder Tiger LifeScience Inc.*)
2008-09	David Dremann (*BS/MS, BME, completed J.D. degree at U. of Illinois 2012*)
2008-12	Luis Solorio (*PhD, BME, currently Assistant Professor, Dept. Of Biomedical Eng. Purdue University*)
2009-11	Angela Carlson (*BS/MS, currently employed at Fenwall Corp. Chicago IL*)
2011-2015	Haoyan (Michael) Zhou (*PhD, BME; currently formulation scientist at Glaxo Smith Kline*)
2013-	Christopher Hernandez (*BS, Boston University; current graduate student in Dept. Biomedical Eng. CWRU*)
2013-	Chawan Manaspon (Ph.D. student, Co-mentored with Dr. Norased Nasongkla at the University of Mahidol, Bangkok, Thailand; Royal Golden Jubilee Fellowship winner)
2014-2015	Monika Goss (*BS/MS student, BME; current Laboratory Manager, Dept. Biomed Eng, CWRU*)
2015-	Selva Jeganathn (BS Penn State Universtiy, *current graduate student in Dept. Biomedical Eng. CWRU*)
2015-	Peter Bielecki (BS Ohio State University, *current graduate student in Dept. Biomedical Eng. CWRU, co-mentor with Dr. Stathis Karathanasis*)
2016- 2017	Frederica Bosca (Visitng scholar, Università di Torino, Dipartimento di Scienza e Tecnologia del Farmaco Torino – Italy)
2016-	Pinunta Nittayacharn (Ph.D. student, M.S. from University of Mahidol, Bangkok, Thailand; Royal Golden Jubilee Fellowship winner)

UNDERGRADUATE

2017-	Chayanan Tensakul (BME, University of Mahidol, Bangkok, Thailand, visitng student)
2017-	Michelle Wiese (BME, CWRU)
2016-	Anshul Dhingra (BME, CWRU)
2016-	Gabriella Fioravanti (BME, CWRU)
2016-	Danielle Gilbert (BME, CWRU) **winner – SOURCE summer fellowship**
2014- 2017	Natalia Gawlik (BME, CWRU)
2014-2015	Alan Burke (BME, CWRU) **winner – PSURG summer fellowship**
2014-2015	Adreinne Damicis (Biology, CWRU)

2013-2014 Laya Bahrani (Chemistry, CWRU)
2013-2015 Anna Gawlik (BME, CWRU)
2013-2015 Pavan Kota (BME, CWRU; currently PhD student at Rice University BME) **winner – SOURCE summer fellowship**
2012 Catherine Cashy (*Summer Researcher, Completing BA in Biology at Denison University*)
2012-2014 Monika Goss (BME, CWRU) **winner – SOURCE summer fellowship**
2011-2013 Mihika Gangoli (BME, CWRU; Washington University graduate school, BME) **winner – WISER summer fellowship**
2011-2013 Divya Sundarapandiyan (BME, CWRU; New York Medical College) **winner – SOURCE summer fellowship**
2011-2013 Eric Silverman (BME, CWRU)
2010-2013 Ashlei Beiswenger (BME, CWRU) **winner – SOURCE summer fellowship**
2010-2012 Alexander Olear (BME, CWRU) **winner – SOURCE summer fellowship**
2010-2013 Sarah Gleeson (BME, CWRU; currently Teach for America volunteer) **winner – SOURCE summer fellowship**
2009 Jesse Hamilton (NSF REU program; currently graduate student in BME at CWRU)
2009-10 Robin Wilson (UG /BME) **winner – SOURCE summer fellowship**
2008 Brett Babin (NSF REU program; Graduate student @ California Institute of Technology)
2008-2009 Angela Carlson (BME, CWRU *; currently employed at Fenwall Corp. Chicago IL*)
2008-2009 Kenneth Nguyen (BME, CWRU ; Data and Process Engineer at Health Diagnostic Laboratory, Inc.) **winner – SOURCE summer fellowship**
2007 Justyna Mach (University of Pennsylvania, Research Assistant)
2007-2009 David Dremann (BME, CWRU ; Associate @ Knobbe Martens Intellectual Property Law Firm) **winner – ACS Silber summer research fellowship**
2006 Amanda Goiffon (BME, CWRU ; Pediatrics Resident @ University of Tennessee Health Center)
2005-2006 Kathi Grammer (BME, CWRU ; industry)
2005-2006 Anukriti Sinha (BME, CWRU ; Medtronics)
2005-2007 Cathy Ruczko (BME, CWRU ; Ohio State University School of Pharmacy –PharmD)
2005-2006 Irina Telyemen (BME, CWRU)
2004-2006 Kevin Chen (BME, CWRU ; Medtronics)
2004-2005 Katherine Scherrer (BME, CWRU)
2004-2005 Jordan Smoke (BME, CWRU)
2003-2005 J. Maxwell Teets (CWRU School of Medicine)
2003-2004 Onkar Dhande (BME, CWRU; Graduate school, Developmental Biology, Baylor School of Medicine)

HIGH SCHOOL
2013 Jimmy Li (Hawken School)
2011-2014 Amanda Keresztesy (Hathaway Brown School)
2009-2011 Jennifer Huang (Hathaway Brown School, currently at Johns Hopkins)
2008-2010 Rebecca Forcier (Hathaway Brown School, currently at Duke University)

RESEARCH ASSISTANT
2017- Reshani Perera (*Research Associate*)
2013-2014 Sandra Mantilla (via CWRU Postbaccalaureate Research Education Program)
2012-2013 Christopher Hernandez (via CWRU Postbaccalaureate Research Education Program)
2011-2012 Angela Carlson
2004-2010 Tianyi M. Krupka
2007 Oliver Small

COMMITTEE MEMBER
2017- Peter Qiao (M.D./Ph.D. program, research advisor ZR Lu, Biomedical Engineering)
2016- Ujjal Didar Singh Sekhon (Ph.D., research advisor Anirban Sen Gupta, Biomedical Engineering)
2016- Aditya Girish (Ph.D., research advisor Anirban Sen Gupta, Biomedical Engineering)

2014-	Nadia Ayat (Ph.D., research advisor ZR Lu, Biomedical Engineering)
2014-	Kihwan Kim (M.S. research advisor M. Gratzl, Biomedical Engineering)
2013-2015	Edgardo Rivera (Ph.D., research advisor – H. von Recum, Biomedical Engineering)
2010-2013	Alyssa Masters (Ph.D., research advisor – A. Sen Gupta, Biomedical Engineering)
2009-2012	Wannarasmi Ketchart (Ph.D. research advisor – M. Montano, Dept. of Pharmacology)
2009-2011	Timothy Wong (M.S. research advisor – A. Sen Gupta, Dept. of Biomedical Engineering)
2008-2009	David Dremann (Primary research advisor, BS/MS Program)
2008-2012	Luis Solorio (Primary research advisor)
2007-2010	Melissa Krebs (Ph.D., research advisor – E. Alsberg, Dept. of Biomedical Engineering)
2006-2008	Yun Zhou (Ph.D., research advisor – C. Deng, Dept. of Biomedical Engineering)
2006-2010	Ravi Patel ((Primary research advisor)
2006-2010	Tianyi Krupka (Primary research advisor)
2005-2007	Brent Weinberg (Primary research advisor)
2004-2005	Paras Parikh (M.S., research advisor – C. Deng, Dept. of Biomedical Engineering)
2004-2005	Elvin Blanco (Ph.D., research advisor – J. Gao, Dept. of Biomedical Engineering)

CURRENT AND PENDING RESEARCH SUPPORT

ACTIVE

R01EB016960 (PI: Exner) NIH /NIBIB *Pressure-driven local drug delivery system for treatment of liver cancer* GOAL: The objective of this proposal is to develop a platform image guided approach for directed local therapy of liver cancer. The strategy relies on bioactive injectable polymer matrixes which can increase drug penetration in the tumor while decreasing the toxic drug levels. Specific Aims: Aim 1: Extending the drug penetration distance; Aim 2: Reducing the effective drug dose and drug resistance; Aim 3: Optimizing the combined system and its characterization in vivo; Aim 4: Evaluating therapeutic efficacy of the optimal delivery system in an experimental model.	5/1/2013-4/30/2018 $1,250,000	3.6 calendar months
DoD CDMRP Prostate Cancer Research IDEA Award W81XWH-16-1-0371 *Early Detection of Prostate Cancer with New Nanoparticle-based Ultrasound Contrast Agents Targeted to PSMA* Role: PD/PI (partnering PI with James Basilion) GOAL: The objective of this research is development of a uniquely capable contrast agent for enhanced detection and delineation of PCa with US using two complementary tactics: 1) detection of PSMA on the surface of prostate cancer cells after targeted NB extravasation and 2) monitoring differences in contrast agent dynamics in tumor versus normal prostate tissue.	9/30/2016-8/31/2019 Total Direct: $750,000 Total Indirect: $457,000	3.6 calendar months
Mary Kay Foundation (MPI with Brady-Kalnay, DiFeo) *PTPmu as a targeting agent for ultrasound-mediated deployment and treatment of ovarian cancer* Role: MPI GOAL: The objective of this research is development of PTPmu targeted, ultrasound sensitive nanobubbles for treatment of advanced ovarian cancer.	7/1/2017-6/30/2019 Total cost: $100,000	No salary support

1 F31 CA200373-01 Principal Investigator: Hernandez, Christopher Role: Research Mentor *Injectable Implants for Increased Tumor Treatment Volume Using Pressure Driven Diffusion*	4/1/2015-12/31/2017	No salary support
1T32EB007509-01 (PI: David Wilson) National Institutes of Health / NIBIB Interdisciplinary Biomedical Imaging Training Program Role: Training faculty member GOAL: To train new interdisciplinary graduate students in the fields of imaging, drug delivery and oncology	9/1/07-8/31/2017	No salary support
ACS Scholars Award (PI: Nicole Steinmetz) *Delivery of Drugs using Targeted Stealth Filaments* Role: Collaborator GOAL: Triple negative breast cancer (TNBC) is an aggressive disease with poor prognoses due to lack of targeted therapies. This proposal sets out to develop a targeted protein therapy making use of a filamentous nanotechnology. The targeted delivery of doxorubicin and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) to TNBC will be studied. If successful, this research would lead to a better treatment of TNBC, a critical unmet clinical need.	1/1/2016-12/31/2020 $792,000	Consultant No salary support
Cancer Imaging Program (Case Comprehensive Cancer Center) Pilot award *Development of Ultrasound Contrast Agents for Molecular Imaging Beyond the Vasculature* GOAL: Use nanobubbles for 1) Targeted early detection of ovarian cancer expressing the CA125 antigen and 2) Molecular detection of prostate specific membrane antigen (PSMA) for detection and biopsy guidance of prostate cancer.	2/1/2016-1/31/2017 $6500	No salary support

PENDING

Case Comprehensive Cancer Center Pilot Grant Program *Immunotherapy Which Triggers Cancer Cell Apoptosis and Boosts Anticancer Cytotoxicity* Goal: Application of local complement inhibition via small molecule inhibitors delivered using drug-eluting injectable polymer implants, combined with systemic potentiation for treatment of unresectable and metastatic cancer.	Submitted 7/23/17	No salary support
UC4DK116236 (MPI: Benninger, U Colorado; Exner) NIH/NIDDK *Ultrasound image-guided therapeutic delivery of immunomodulatory and anti-apoptotic agents into the diabetic islet microenvironment* Role: MPI Goal: Development of nanobubbles for therapeutic delivery and monitoring treatment response for prevention of type 1 diabetes.	9/1/2017-8/30/2021 Total direct: $836,465 Total indirect: $395,769	2.4 calendar months

NIH/NIBIB (MPI: Exner, Basilion) *Nanoparticle-based ultrasound contrast agents targeted to PSMA for biopsy guidance and staging of prostate cancer* Submitted 4/12/2017 Goal: The objective of this project is to optimize PSMA-targeted nanobubbles for US imaging of prostate cancer. Specifically we will: 1) characterize NB parameters in human PCa lines (e.g. bubble echogenicity and stability, specificity and longevity of cell targeting); and 2) compare the US detection properties of PSMA-targeted NB to microbubble agents (Definity® microbubble) in in vivo PCa models.	TBD Total Direct: $ 1,753,350.00 Total Indirect: $ 822,384.00	3.6 calendar months
T32 Training Grant NIH/NCI *Integrated Cancer Nanotechnology Research Training Program* Role: PD/PI (MPI with Ruth Keri) Submitted 5/25/2017 GOAL: Cancer nanomedicine has immense potential to revolutionize personalized medicine and human health. This focused training grant for postdoctoral fellows will shape the next generation of scientists who will be able to integrate the scientific and engineering skills with clinical needs and with ability to translate their technologies to actual useable applications.	12/1/2017-11/30/2022 Total Direct: $1,711,440 Total Indirect: $126,115	No salary support
NIH/NIBIB (PI: Exner) *Drug-Loaded Nanobubbles for Ultrasound Enhanced Delivery to Colon Cancer Liver Metastasis* Submitted 4/11/2017 Goal: To address the urgent need for more effective treatment strategies for liver metastasis from colorectal cancer, this project will develop a new nanotechnology-based drug delivery technology which can be visualized and deployed at the tumor sites in real time using ultrasound.	Total direct costs: $1,640,208	3.0 calendar months
NIH / NCI (PI: Sanjay Gupta, MPI, Project lead: Exner) 1P01CA210942-01A1 Submitted 5/25/2017 *Precise Drug Delivery Technologies Targeting Cancer Metastasis* Role: MPI/ Project Lead GOAL: The primary objective of the program is to develop precise drug delivery platforms to target metastases of the most common forms of human cancers of different organ sites.	2/1/2018-1/31/2023 Total costs: $5,783,892	1.2 calendar months

The project on the P01 has overlap with the R01 project above. Proposals which are part of complex program project grants are permitted to be submitted as standalone R01s as per **https://public.csr.nih.gov/applicantresources/receiptreferal/pages/evaluation-of-unallowable-resubmission-and-overlapping-applications.aspx**

NSFC (National Natural Science Foundation China) PI: Yuanyi Zheng, MD, PhD, Shanghai Jiaotong University Role: Co-Investigator *Artificially Engineered "Tumor Bio-magnet" for Collecting Blood-Circulating Phase Transitional Nanoparticles for Tumor Imaging and Therapy*	7/1/2017-6/30/2022 3,000,000 RMB	No salary support (will provide shared postdoc)

1R01CA211171-01 (Brady-Kalnay, Exner, DiFeo MPI) *PTPmu as a targeting agent for ultrasound-mediated deployment and treatment of ovarian cancer* Role: MPI GOAL: The objective of this research is development of PTPmu targeted, ultrasound sensitive nanobubbles for treatment of advanced ovarian cancer.	Under development Total Direct: $ 2,464,881 Total Indirect: $ 1,441,955	3.6 calendar months
NIH/NIBIB (MPI: Exner, Kolios, Ryerson U) Role: MPI *Improving Local Drug Delivery to Tumors Using Ultrasound and Photoacoustics* To be submitted 8/12/2017 The overarching goal of this proposal is to develop a practical, externally controlled strategy to enhance the performance of injectable drug delivery systems for local treatment of inoperable solid tumors. This represents a novel ultrasound application in enhancing delivery from intratumoral drug-eluting implants.	12/1/2017-11/30/2021 Total Direct: $1,992,807	3.6 calendar months

COMPLETED

CWRU CTSC Pilot Grant (Brady-Kalnay, Exner, DiFeo MPI)
PTPmu Targeting of Nanobubbles and Ultrasound Guided Therapy for Ovarian Cancer
06/01/16 to 05/31/17
Total Direct: $50,000
Goal: The objective of this research is development of PTPmu targeted, ultrasound sensitive nanobubbles for treatment of advanced ovarian cancer.

OC110149 WX81XWH-12-1-0500 (PI: Exner)
CDMRP Ovarian Research Program Pilot Grant, Department of Defense
9/30/2012-9/29/2015
Development of Nanobubble Ultrasound Contrast Agents for Molecular Imaging and Early Detection of Ovarian Cancer
Goal: Development of a contrast agent for early detection of ovarian cancer with US using two complementary tactics—detection of CA-125 on the surface of ovarian cancer cells after targeted NB extravasation and monitoring of differences in contrast agent dynamics in tumor versus normal ovary tissue.

R01CA136857 (PI: Exner)
National Institutes of Health / NCI
5/1/2009 - 1/30/2015
Sensitizer Delivery for Focused Hyperthermia Cancer Treatment
Goal: To develop ultrasound visible, externally modulated nanoparticles for delivery of Pluronic as a thermal sensitizer for tumor thermal ablation.

S10OD016164-01 (PI: Patricia Conrad)
National Institutes of Health
Acquisition of a Leica TCS SP8 Confocal Microscope for a Multi-User Facility
7/15/2013-7/14/2014
$597,379
Role: major user

Department of Defense Postdoctoral Fellowship (PI: Luis Solorio)
Chemotaxis Driven Treatment to Reduce Metastasis Post Surgical Resection of Breast Cancer
9/1/2012 – 8/31/2013

Role: Mentor (co-mentor William Schiemann, Case Comprehensive Cancer Center)

Pilot funding for Image-guided Biomaterials Development (PI: S Rowan, Dept. of Macromolecular Science and Engineering)
Institute for Advanced Materials, CWRU
Noninvasive characterization of in situ modulus changing implants using diagnostic ultrasound
2/1/2012-1/31/2013
Role: Co-PI

R21CA131014 (PI: Exner)
National Institutes of Health / NCI
Use of Vasoactive Agents to Enhance Radiofrequency Ablation
2/1/2010 - 1/31/2013

R01CA118399 (PI: Exner)
National Institutes of Health / NCI
8/1/2006 - 7/31/2012
Functional Polymer Matrixes for Site-Specific Image Guided Drug Delivery

R01CA118399 - supplement (PI: Exner)
National Institutes of Health / NCI
8/1/2008 - 7/31/2012
Supplement to cover tuition and stipend for underrepresented minority graduate student

CWRU Challenge Grant Award (Co-PI, PI: A Abramson, Dept. Mech. Eng)
Johnson & Johnson / CWRU
Oncology Therapeutics: Hyperthermia using self-heating nanoparticles in conjunction with Pluronic nanobubbles
7/1/2010-8/31/2012

Supplement to 5P30 043703-17S3 to (PI: S Gerson, PD: JR Haaga)
National Institutes of Health / NCI
10/1/2005 - 3/31/2012
Vascular modulation with or without chemotherapy for enhancement of RF ablation;
Role: Co- Investigator

2010 SIR Foundation Grant (PI: Luke Wilkins, Radiology Resident)
Society for Interventional Radiology
Evaluation of Pharmacologic Agenst Modulating Tumor Blood Flow: Effect on Thermal Ablation Size
7/1/2010-12/1/2010
Role: Co-Mentor

Biomedical Research and Technology Transfer Program (BRTT) Pilot Research Grant
Case Western Reserve University
10/1/2007 – 6/1/2009
Nanobubble-Nanoparticle Complexes for Ultrasound Imaging and Drug Delivery

R21DE17165 (PI: Yiping Han, School of Dentistry, CWRU) NIH/NIDCR
Sonoporation as a new genetic tool for F. nucleatum.
8/1/2007-7/31/2009
Role: Co-investigator; Person Months 0.6
The major goals of this project are to investigate the mechanism of sonoporation in F. nucleatum in order to ultimately to develop it into a powerful genetic tool to streamline mutant construction in bacteria.

CWRU Center for Stem Cell and Regenerative Medicine (PI: B. Hoit and M. Costa, Dept. of Cardiology)
1/1/2008-12/31/2009
Novel platform for targeted delivery of stem cells via coupled microbubble-stem cell complexes and ultrasound mediated bubble destruction.
Role: Co-investigator

Presidential Research Initiative Grant (PI: Exner)
Case Western Reserve University
7/1/2005 - 6/30/2008
Ultrasound-Mediated Drug Delivery
Role: Principal Investigator

National Institutes of Health (PI: C. Deng, Dept. of Biomedical Engineering)
9/1/2005-2/28/2007
Sonoporation Effects of Therapeutic Ultrasound;
Role: Co-investigator

1R21EB002847 (PI: Exner)
National Institute of Biomedical Imaging and Bioengineering /NIH
9/30/2003 - 8/31/2006
Image-guided Chemotherapy and Radiofrequency Ablation

Cuyahoga Area Pilot Research Award (PI: Exner)
American Cancer Society, Ohio Division, Inc.
7/1/2003 - 6/30/2005
Injectable Polymer Gels as Delivery Matrixes and Sensitizers for Local Chemotherapy

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PUBLICATIONS

**** indicates equal contributions (co-first authorship)***

1. Bing C, Hong Y, Hernandez C, Munaweera I, Rich M, Szczepanski D, Bolding M, **Exner AA**, Corbin I, Chopra R. Acoustic emissions during blood-brain barrier disruption with focused ultrasound and real-time feedback control. In preparation.

2. Yuan H*, Hernandez C*, Bielecki P, Perera RH, Gao Y, Zhou H, **Exner AA.** Ultrasound-triggered Nanobubbles for Tumor Therapy. In preparation.

3. Bosca F, Bielecki P, Barge A, **Exner AA.** Design of porphyrin-loaded crosslinked Pluronic nanobubbles for sonodynamic therapy. In preparation.

4. Hernandez C*, Gulati S*, Stewart P, **Exner AA**. Cryo-EM Visualization of Lipid and Polymer-Stabilized Perfluorocarbon Gas Nanobubbles . *Nanoscale.* Under Review.

5. Manaspon C, Hernandez C, Nasongkla N, **Exner AA.** Improving Distribution of Fluorescein Released from *In Situ* Forming PLGA Implants Using Therapeutic Ultrasound. *Annals of Biomedical Engineering*. Under revision.

6. Gao Y*, Hernandez C*, Wu H, Perera R, Kota P, Burke A, Zhang H, **Exner AA.** Ultrasound Molecular Imaging of Ovarian Cancer with CA-125 Targeted Nanobubble Contrast Agents. *Nanomedicine: NBM*. 2017. Accepted. In press. PMID: 28603079

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8. Hernandez C, Goss M, Gawlik A, Zhou H, Hernandez C, **Exner AA.** Macroporous Acrylamide Phantoms Improve Prediction of In Vivo Performance of In Situ Forming Implants" *Journal of Controlled Release*. 2016 Oct 11. 243:225-231. doi: 10.1016/j.jconrel.2016.10.009. PMID: 27742445.

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10. Perera R, Wu H, Hernandez C, Zheng H, Burke A, **Exner AA**. Formulation and Characterization of a New Stabilized Nanobubble Ultrasound Contrast Agent. *Nanomedicine: Nanotechnology, Biology, and Medicine*. 2017. 13(1):59-67. PMID: 27565686

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PUBLISHED CONFERENCE PROCEEDINGS PAPERS

1. Jeganathan S, Gilbert D, Hernandez C, Tavri S, Exner AA. Ultrasound Characterization of Slow Precipitating Implants for Vascular Occlusion. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

2. Nieves L, Exner AA. Effect of the Surfactant Pluronic on the Stability of Lipid-Stabilized Perfluorocarbon Nanobubbles. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

3. Hernandez C Exner AA. Ultrasound Signal from Sub-Micron Lipid-coated Bubbles. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

4. Hernandez C, Gulati S, Stewart P, Exner AA. On the Fate of Mesh-stabilized Lipid Nanobubbles after Destruction with Ultrasound. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

5. Lilly J, Xia H, Ankher A, Ramamamurthy G, Basilion J, Exner AA. Nanobubble Contrast Agents Enhance Ultrasound Imaging of Prostate Tumors in Mice. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

6. Bielecki P, Hernandez C, Jeganathan S, Manaspon C, Kolios MC, Exner AA. Enhancing Fluorescein Release from *In Situ* Forming PLGA Implants using Therapeutic Ultrasound. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

7. Brendl E, Hysi E, Hernandez C, Exner AA, Kolios MC. Using ultrasound and photoacoustics to monitor in situ forming implant structure and drug release. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

8. Jafari Sojahrood A, Nieves L, Hernandez C, Exner AA, Kolios MC. Theoretical and experimental investigation of the nonlinear dynamics of nanobubbles excited at clinically relevant ultrasound frequencies and pressures: the role of lipid shell buckling. IEEE International Ultrasonics Symposium 2017 Annual meeting. *In preparation.*

BOOK CHAPTERS

1. Solorio L, Zhou H, Carlson A, **Exner AA.** Bioedegradable Polymeric Implants. In Engineering Polymer Systems for Improved Drug Delivery , Bader R and Putnam D Eds. John Wiley & Sons, Inc., Hoboken, NJ. 2014; ISBN: 978-1-118-09847-9

2. Solorio L, Solorio L, Olear A, Gleeson S, Carlson A, **Exner AA**. Phase Inverting Polymer Systems in Drug Delivery and Medicine. In Polymer Phase Behavior. Nova Science Publishers. Ehlers TP and Wilhelm JK Eds*. 2012;* ISBN: 978-1-61324-336-7

3. Krupka TM, **Exner AA.** "Nanobubbles and their putative application to cancer medicine", Nanomedicine and Cancer. Srirajaskanthan R, Preedy VR Eds., CRC Press/Taylor & Francis Science Publishers, 2011. ISBN*:* 9781578087273

4. **Exner AA,** Gao J, Stowe NT, "Techniques in X-Ray Computed Tomography in the Evaluation of Drug Release Systems & Their Application" in Medical Imaging Systems: Technology and Applications, World Scientific Publishing Co. Pte. Ltd., 2006. ISBN: 9812569898

PATENTS AND INVENTION DISCLOSURES

1. Drug delivery devices and methods; Inventors: Gao, Jinming; Qian, Feng; Exner, Agata; Haaga, John R.; Filed October 4, 2002.

2. Use of Diamox for improvement of lesion detection on Imaging Studies, and differentiation of benign and malignant tumor masses; Inventors: Haaga, John; Exner, Agata; Stow, Nicholas

3. Nontoxic sensitizing pretreatment for improved radiofrequency ablation of tumors; Inventors: Exner, Agata; Krupka, Tianyi; Weinberg, Brent; Haaga, John; Utility patent filed Nov. 2007.

4. Method of detecting cancer; Inventors: Haaga, John; Haaga, Timothy; Exner, Agata; Stowe, Nicholas. Patent filed July 2007.

5. Nanobubble-nanoparticle composite vehicles for imaging and targeted drug delivery; Inventors: Exner, Agata, von Recum Horst, Zheng Yuanyi. Invention disclosure submitted November 2007.

6. Noninvasive characterization of drug delivery systems using diagnostic ultrasound; Inventors: Exner A, Solorio L, Mach J, Patel R. Invention disclosure submitted April 2009.

7. Novel formulation technique of nanobubble ultrasound contrast agents; Inventors: Exner A, Krupka T, Solorio L. Invention disclosure submitted July 2009. Utility patent submitted Sept. 2011

8. Advanced Applications for Bioactive Pluronics; Inventors: Agata Exner, Bryan Traughber. Provisional patent in preparation.

9. USPT 9,320,757 Exner, et al. **Issued April 26, 2016** Method for treating a neoplastic disorder

10. US PCT Application "Stabilized Nanobubbles For Diagnostic And Therapeutic Applications", Application No: PCT/US2011/053272, Filing Date: 09/26/2011, Inventors: Agata Exner, Tianyi Krupka and Luis Solorio, CWRU: 2010-1767

11. Invention Disclosure, "Mechanically Induced Convective Enhanced Delivery System" by Case No. 2012-2220.

12. "Toxicity Enhancing Compounds And Methods", Application No: 13/415,538, Filing Date: March 8, 2012, CWRU Ref. 2011-1992 United States Patent 9,132,149 **issued September 15, 2015**

INVITED LECTURES AND SEMINARS

1. "Echogenic Nanobubbles: New opportunities for ultrasound-enhanced drug delivery for cancer therapy"; Invited speaker, Nanotech 2016 Conference & Expo, Washington D.C., May 2017

2. "Echogenic Nanobubbles: New opportunities for US molecular imaging and US-enhanced drug delivery beyond tumor vasculature "; Center for Ultrasound Molecular Imaging and Therapeutics, University of Pittsburg School of Medicine, February 2017

3. "Nanobubble Ultrasound Contrast Agents for Cancer Detection and Targeted Drug Delivery"; Dept. of Pharmaceutical Sciences, University of Colorado, Denver, November 2016

4. "Nanobubble Ultrasound Contrast Agents for Cancer Detection and Targeted Drug Delivery", Invited speaker, CNRS Centre de Biophysique Moléculaire (CBM), Orleans, France, September 2016

5. "Nanobubble Ultrasound Contrast Agents for Cancer Detection and Targeted Drug Delivery", Invited speaker, Dept. of Physics, Ryerson University, Toronto Canada, July 2016.

6. "Nanobubble Ultrasound Contrast Agents for Cancer Detection and Targeted Drug Delivery", Invited speaker, Nanotech 2016 Conference & Expo, Washington D.C., May 2016

7. "Molecular Imaging Beyond the Vasculature with New Nano Ultrasound Contrast Agents", Invited speaker, 3rd International Conference of Chinese Society of Ultrasound Molecular Imaging (CSUMI), Chongqing, China, April 2016

8. "Magic Bubbles – How nanotechnology is shaping the future of ultrasound imaging", Invited speaker, Community Salon Series, Magnificat High School, Rocky River, OH January 12, 2016

9. "Ultrasound-Mediated Drug Delivery in Cancer Therapy", Invited speaker, Dept. of Biomedical Engineering University of Mahidol, Salaya, Thailand August 2015

10. "Magic Bubbles: Sensitizing Nanoparticles for Targeted Enhancement of Tumor Thermal Ablation and Radiotherapy ", Invited speaker, Society for Thermal Medicine Annual Meeting, April 2015

11. "Ultrasound-Mediated Drug Delivery in Liver Cancer Treatment", Case Center for Imaging Research seminar, CWRU, 2015

12. "From Bubbles to Blobs: New Approaches to Cancer Drug Delivery", Department of Biomedical Engineering Biomaterials Seminar, 2014

13. "From Bubbles to Blobs: New Approaches to Cancer Drug Delivery", SOURCE undergraduate summer fellowship weekly seminar, 2014

14. "Ultrasound mediated drug delivery for cancer therapy", Department of Biomedical Engineering, University Hospitals of Cleveland, Dept. of Radiology Grand Rounds, March 25, 2014

15. "Grants*woman*ship - Practical Tips for Getting (and Staying!) Funded ", CWRU Women Faculty School of Medicine program, March 24 2014

16. "Oncologic Image Guided Drug Delivery", CWRU Cancer Imaging Program Retreat, October 2013

17. "Ultrasound mediated drug delivery for cancer therapy", Department of Biomedical Engineering, The University of Akron, Akron OH, September 20, 2013

18. "An Insider's Perspective: How to Step Out From Under Your Mentor's Shadow and Stand On Your Own Two Feet as a Researcher", Case Comprehensive Cancer Center Retreat, July 2011

19. "Image-guided Drug Delivery in Cancer Chemotherapy", Case Comprehensive Cancer Center, February 11, 2011

20. Cleveland Science Café "Drug delivery in cancer therapy", Nov. 2010

21. "Image-guided Drug Delivery in Cancer Therapy" Department of Radiology Grand Rounds, CWRU, November 3, 2009

22. "Image-guided Drug Delivery" National Biomaterials Advisory Board Roundtable on Biomedical Engineering Materials and Applications (BEMA), Woods Hole, MA, July 16, 2009

23. "Image-guided Drug Delivery" Department of Pharmacology, CWRU, November 4, 2008

24. "Nanobubble-nanoparticle composite vehicles for imaging and drug delivery", Nanotechnology Summit, Cleveland, OH, September 2008

25. "Pills and Needles are *SO* 20th Century", CWRU orientation, August, 2008

26. "Interventional Oncology: Opportunities for Drug Development and Delivery" Department of Pharmaceutical Sciences, School of Pharmacy, University of Michigan, Ann Arbor, March 12, 2008

27. "Use of Vasoactive Drugs to Facilitate RF Ablation in a Rat Model", Department of Radiology Seminar Series, Case Western Reserve University, April 11, 2007

28. "Image-guided Interventions in Oncology: Opportunities for Drug Development and Delivery", Department of Pharmaceutical Sciences, School of Pharmacy, University of Wisconsin, Madison, February 22, 2007

29. "Pills and Needles are *SO* 20th Century", CWRU orientation, August 24, 2006

30. "Image-guided Drug Delivery Approach to Local Cancer Chemotherapy", Case BRTT meeting, June 28, 2006

31. "Development of Functional Polymer Matrixes for Image Guided Drug Delivery", Frontiers in Biomedical Imaging Seminar Series, Department of Biomedical Engineering, Case Western Reserve University School of Medicine, March 18, 2005.

32. "Image Guided Drug Delivery: CT and Local Chemotherapy", Journal Club, Department of Radiology, Case Western Reserve University School of Medicine, March 19, 2004.

33. "Image Guided Drug Delivery: New Applications of Old Concepts", Grand Rounds (invited speaker), Department of Radiology, University Hospitals of Cleveland, March 4, 2004.

CONFERENCE PRESENTATIONS

9. C. Bing, Y. Hong, C. Hernandez, I. Munaweera, M. Rich, D. Szczepanski, M. Bolding, A. Exner, I. Corbin, R. Chopra. Acoustic emissions during blood-brain barrier disruption with focused ultrasound and real-time feedback control. 2017. International Society for Therapeutic Ultrasound meeting. *Oral presentation*.

10. C Hernandez, L Nieves, J Lilly, H Xia, A Ankher, X Wang, G Ramamurthy, R Advincula, J Basilion, MC Kolios, AA Exner. Toward successful ultrasound molecular imaging of cancer with nanobubble contrast agents. Contrast Media Research 2017. *Under review.*

11. Amin Jafari Sojahrood, Lenitza Nieves, Christopher Hernandez, Agata A. Exner, Michael C. Kolios. Theoretical and experimental investigation of the nonlinear dynamics of nanobubbles excited at clinically relevant ultrasound frequencies and pressures: the role of lipid shell buckling. Contrast Media Research 2017. *Under review.*

12. Gabriella Fioravanti, Christopher Hernandez, Agata A. Exner. Lipid Acyl Chain Length Improves Stability of Nano-sized Ultrasound Contrast Agents In Vitro. Biomedical Engineering Society 2017 meeting. Under review.

13. Pinunta Nittayacharn, Jacob Lilly, Agata A Exner. Maximizing Drug Loading in Microbubbles for Ultrasound - Mediated Drug Delivery. Biomedical Engineering Society 2017 meeting. *Under review.*

14. Selva Jeganathan, Christopher Hernandez, Anshul Dhingra, Agata Exner. Overcoming Inherent Chemotherapeutic Resistance of Liver Cancer through Concurrent Intratumoral Delivery of Drug and Chemosensitizer. Biomedical Engineering Society 2017 meeting. *Under review.*

15. Danielle Gilbert, Selva Jeganathan, Sidhartha Tavri,Agata A. Exner. Reducing Implant Precipitation Rate for Deeper Vascular Occlusion. Biomedical Engineering Society 2017 meeting. *Under review.*

16. Jeganathan S, Gilbert D, Hernandez C, Tavri S, Exner AA. Ultrasound Characterization of Slow Precipitating Implants for Vascular Occlusion. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*

17. Nieves L, Exner AA. Effect of the Surfactant Pluronic on the Stability of Lipid-Stabilized Perfluorocarbon Nanobubbles. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*

18. Hernandez C Exner AA. Ultrasound Signal from Sub-Micron Lipid-coated Bubbles. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*

19. Hernandez C, Gulati S, Stewart P, Exner AA. On the Fate of Mesh-stabilized Lipid Nanobubbles after Destruction with Ultrasound. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*

20. Lilly J, Xia H, Ankher A, Ramamamurthy G, Basilion J, Exner AA. Nanobubble Contrast Agents Enhance Ultrasound Imaging of Prostate Tumors in Mice. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Oral presenation.*

21. Bielecki P, Hernandez C, Jeganathan S, Manaspon C, Kolios MC, Exner AA. Enhancing Fluorescein Release from *In Situ* Forming PLGA Implants using Therapeutic Ultrasound. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*

22. Brendl E, Hysi E, Hernandez C, Exner AA, Kolios MC. Using ultrasound and photoacoustics to monitor in situ forming implant structure and drug release. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Oral presentation.*

23. Jafari Sojahrood A, Nieves L, Hernandez C, Exner AA, Kolios MC. Theoretical and experimental investigation of the nonlinear dynamics of nanobubbles excited at clinically relevant ultrasound frequencies and pressures: the role of lipid shell buckling. IEEE International Ultrasonics Symposium 2017 Annual meeting. *Poster presentation.*

24. Wu H, Perera R, Exner AA. Pharmacokinetic Analysis and Extravasation Study of a Novel Nanobubble Ultrasound Contrast Agent. Radiological Society of North America 2016 Meeting. *Digital Poster Presentation;* ***RSNA Trainee Research Prize***

25. Nieves L, Hernandez C, Exner AA. Structure-Function Relationship between Lipid Shell Components and Surface Tension of Nanobubble Ultrasound Contrast Agents; 2016 Annual Biomedical Research Conference for Minority Students (ABRCMS) Tampa, FL; *Poster Presentation*

26. Gawlik N, Hernandez C, Exner AA. Increasing Penetration of In Situ Forming Implants through Incorporation of Osmotic AgentsSFB Midwest 2016, *Oral presentation*

27. Nieves L, Hernandez C, Exner AA. Structure-Function Relationship between Lipid Shell Components and Surface Tension of Nanobubble Ultrasound Contrast Agents; SFB Midwest 2016, *Oral presentation;* ***Honorable Mention Award***

28. Gilbert D, Hernandez C, Exner AA. Macroporous Phantom Gel for Improved In Vivo-In Vitro Correlation of In Situ Forming Polymer Implants SFB Midwest 2016, *Oral presentation*

29. Overcoming Chemotherapeutic Resistance in Colorectal Carcinoma Tthrough Concurrent Intratumoral Delivery of Therapeutic and a Chemosensitizer; Dingha A, Jeganathan S, Hernandez C, Exner AA; SFB Midwest 2016, *Oral presentation*

30. Fioravanti G, Hernandez C, Exner AA, Lipid Acyl Chain Length Improves Nanosized Contrast Agents Stability In Vitro; SFB Midwest 2016, *Oral presentation*

31. Bosca F, Bielecki P, Hermandez C, Barge A, Exner A. Design of Porphyrin-Loaded Nanobubbles for Theranostic Applications, *Poster presentation*; 2016 XXIV EFMC International Symposium on Medicinal Chemistry.

32. Manaspon C, Hernandez C, Nasongkla N, Exner AA. Improving Distribution of Agents Released from PLGA Implants Using Therapeutic Ultrasound. *Oral Presentation* at 2016 BMES Conference.

33. Jeganathan S, Hernandez C, Gawlik N, Exner AA. Macro-porous Phantom for Improved In Vitro-In Vivo Correlation for Mock Drug Release Kinetics for In Situ Forming Polymer Implants. *Oral Presentation* at 2016 BMES Conference.

34. Hernandez C, Wang X, Basilion J, Exner AA. Early Detection of Prostate Cancer with New Nanoparticle-Based Ultrasound Contrast Agents Targeted to PSMA. 2016 World Molecular Imaging Conference. *Poster presentation.*

35. Hernandez C, Mantilla S, von Recum HA, Exner AA. Design of Reloadable In Situ Forming Implants for Delivery of Doxorubicin. 2016 World Biomaterials Congress. *Oral Presentation*.

36. Gawlik N, Hernandez C, Exner AA. Mechanical Properties of Injection Site Govern Performance of In Situ Forming Polymer Implants. 2016 World Biomaterials Congress. *Oral Presentation*.

37. Patel R, Perera R, Oleinick NL, Exner AA. Pluronic Coblock Polymer L10 Demonstrates Promise As Novel Radiosensitizing Agent for Human Colorectal Cancer. ASTRO 2015; Article in INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY, BIOLOGY, PHYSICS 93(3):E531-E532 · 2015

38. Stukel J, Goss R , Exner AA, Willits R. Development of Clinical Ultrasound Technique for Analysis of Protein Content Within Hydrogels. Summer Biomechanics, Bioengineering and Biotransport Conference. June 17-20, 2015. *Poster presentation*

39. Goss R, Stukel J, Willits R, Exner AA. Development of a High-Throughput Ultrasound Technique for the Analysis of Tissue Engineering Constructs. Society for Biomaterials Annual Meeting 2015, *Oral presentation*

40. Gawlik A, Zhou H, Exner AA. Three-dimensional ultrasound for non-invasive characterization of in situ forming implants: a validation study. Midwest BME Career Conference 2014. *Poster presentation*

41. Goss R, Stukel J, Willits R, Exner AA. Development of a High-Throughput Ultrasound Technique for the Analysis of Tissue Engineering Constructs. Biomaterials Day 2014, University of Kentucky. *Poster presentation*

42. Goss M, Zhou H, Exner A. Development of Tissue Equivalent Phantoms for Ultrasound Elastography Characterization of In Situ Forming Implants. SOURCE Symposium and Poster Session, Cleveland, April 2014, Poster presentation.

43. Kota P, Hernandez C, Exner AA. Formulation and In vitro Analysis of Targeted Lipid-Pluronic Nanobubbles. Biomedical Engineering Society Annual Meeting, October 2014. *Oral presentation*

44. Zhou H, Goss M, Gawlik A, Exner AA. Noninvasive Evaluation of the Role of Polymer Molecular Weight on Erosion and Degradation of *In Situ* Forming Implants, Controlled Release Society National meeting, July 2014. *Poster presentation*

45. Hernandez C, Kota P, Exner AA. Stiffness of Injection Site Increases Penetration Distance of Drug Released from Release of *In Situ* Forming Polymer Implants, Controlled Release Society National meeting, July 2014.

Poster presentation

46. Perera R, Kota P, Exner AA. Formulation of Stabilized Ultrasound Visible Nanoparticles for Thermal Sensitizer Delivery, Controlled Release Society National meeting, July 2014. *Poster presentation*

47. Goss M, Zhou H, Exner AA. Development of Tissue Equivalent Phantoms for Improved In Vitro Characterization of *In Situ* Forming Drug Delivery Implants, Controlled Release Society National meeting, July 2014. *Poster presentation*.

48. Hernandez C, Solorio L, Exner AA. Development of a Novel Release Phantom for Improved In Vitro-In Vivo Correlation of Drug Release From In Situ Forming Polymer Implants. Society for Biomaterials National Meeting, April 2014 *Oral presentation,* ***Star Student Award Winner*.**

49. Zhou H, Goss M, Gawlik A, Exner AA. Noninvasive Characterization of Polymer Degradation and Erosion using Ultrasound Elastography (UE), Society for Biomaterials National Meeting, April 2014 *Oral presentation*

50. Zhou H, Goss M, Gawlik A, Exner AA. Noninvasive Characterization of Polymer Degradation and Erosion using Ultrasound Elastography (UE), Society for Biomaterials Regional Meeting, October 2013.

51. Gleeson S, Solorio L, Exner AA. Degradation of Ultrasound Contrast Agents Embedded in a Tissue Phantom, to the Society For Biomaterials 2013 Annual Meeting and Exposition

52. Wu H, Rognin NG, Perera R, Guenette G, Sanders C, Exner AA, Haaga JR, Evaluation of the microcirculation and perfusion of a rat liver tumor model after transarterial embolization using contrast-enhanced ultrasonography and perfusion analysis. 2013 Society for Interventional Radiology meeting.

53. Sundarapandiyan D, Solorio L, Exner AA. Effect of BSA and DiI on Drug Release from In Situ Forming Polymer Implants BMES Annual Meeting 2012

54. Beiswenger A, Kakish C, Solorio L, Abramson A, Exner AA. Development of Self-Heating Microparticles for Transarterial Embolization and Tumor Ablation Therapy. BMES Annual Meeting 2012

55. Toy R, Vicente P, Tran E, Lin D, Einstein J, Hayden E, Camann A, Berman Z, Wuttisarnwattana P, Meyers J, Wu H, Exner A, Basilion J, Wilson D, Karathanasis E, The unique voyage of nanoparticles in tumor microcirculation, BMES 2012 Annual Fall Meeting, Atlanta, GA *(Oct 2012 - upcoming); Oral presentation*

56. Solorio L, Exner AA. Noninvasive Imaging Characterization of In Situ Forming Implants with Diagnostic Ultrasound. Society For Biomaterials Fall Symposium, *accepted for poster presentation*, October 2012

57. Solorio L, Sundarapandiyana D, Olear A, Beiswenger A, and Exner A. Altering the Release Kinetics of In Situ Forming Polymer Implants with the Addition of BSA and DiI. Society for Biomaterials, 9th World Congress, China*; Poster presentation,* July 2012.

58. Wilkins L, Wu H, Traughber B, Haaga J, Exner AA. Radiofrequency ablation: effect of tumor and organ-specific pharmacologic modulation of arterial and portal venous blood flow on coagulation diameter in a N1-S1 tumor model. Oral presentation at Society for Interventional Oncology Meeting, March 25 2012.

59. Wu H, Krupka TM, Traughber B, Wilkins L, Perera R, Haaga J, Exner AA. Contrast-enhanced ultrasound for image guidance and real-time treatment monitoring of radiofrequency ablation: a preliminary investigation. Radiological Society of North America 2011 meeting, Nov. 2011. *Oral presentation*

60. Beiswenger A, Solorio L, Exner AA. Differentiating In Vivo and In Vitro Polymer Implant Drug Release.

Regional meeting of the Society for Biomaterials., Purdue University, Oct 2011. *Oral presentation*

61. Sundarapandiyan D, Solorio L, Exner AA. Effect of BSA/Dii Concentration on Polymer Implant Drug Release. Regional meeting of the Society for Biomaterials., Purdue University, Oct 2011. *Poster presentation*

62. Olear A, Solorio L, Exner AA. Using ultrasound to predict drug release from injectable implants. Regional meeting of the Society for Biomaterials., Purdue University, Oct 2011. *Poster presentation*

63. Solorio L, Olear A, Beiswenger A, Hamilton J, Patel R, **Exner AA.** The Role of PLGA Molecular Weight Blends on the Phase Inversion, Drug Release, and Erosion of *In Situ* Forming Implants. 2011 Controlled Release Society meeting. *Poster presentation*

64. Carlson A, **Exner AA.** Release and Uptake of Pluronic from In Situ Forming PLGA Implants. Society for Biomaterials 2011 meeting Society for Biomaterials 2011 meeting. *Poster presentation.*

65. Solorio L, Olear A, Beiswenger A, Hamilton J, Patel R, **Exner AA.** The role of varying PLGA molecular weight blends drug release and phase inversion. Society for Biomaterials 2011 meeting. *Oral presentation.*

66. Wu H, Patel R, Krupka T, Zhang Y, Solorio L, **Exner AA.** Differentiation of benign periablational enhancement from residual tumor with contrast-enhanced ultrasonography following radiofrequency ablation in an experimental rodent model of colorectal cancer. Society for Interventional Radiology 2011 meeting. *Oral presentation.*

67. Carlson A, **Exner AA**. Release and Uptake of Pluronic from In situ-forming PLGA Implants. Regional meeting of the Society for Biomaterials. Cleveland OH, Nov. 2010

68. Olear A, Solorio L. **Exner AA.** Effect of Varying PLGA Molecular Weight Blends on Small-Molecule Drug Release, Regional meeting of the Society for Biomaterials. Cleveland OH, Nov. 2010

69. Huang J, **Exner AA.** The Effect of Pluronic and Hyperthermia on Cancer Cell Permeability, BMES 2010 annual meeting

70. Olear A, Solorio L. **Exner AA.** Effect of Varying PLGA Molecular Weight Blends on Small-Molecule Drug Release, BMES 2010 annual meeting, ***Student Travel Award Winner***

71. Patel B, Solorio L, Wu H, Krupka T, **Exner AA**, Gerald Saidel. Model analysis of implant formation and drug release from *in situ* forming implants, BMES 2010 annual meeting

72. Krupka T, Wilson R, Wu H, **Exner A**. Development of Echogenic Nanobubbles for Ultrasound Molecular Imaging. 2010 World Molecular Imaging Congress (WMIC 2010), September 8-11, 2010 in Kyoto, Japan. Poster presentation. ***Student Award Winner***

73. Solorio L, Patel R, **Exner AA.** Noninvasive Characterization of In situ Forming Implants Using Ultrasound. Controlled Release Society meeting, Portland, OR July 2010. *Poster presentation*

74. Ravi B. Patel, Luis Solorio, Hanping Wu, Tianyi Krupka, **Agata A. Exner.** Characterization of in vivo drug release from in situ forming drug delivery implants. 2010 Society of Biomaterials Annual Meeting, Seattle, Washington - *Podium presentation.*

75. Krupka TM, Wilson RE, Solorio L, Wu H, Azar N, **Exner AA,** Development of Multifunctional Lipid-Pluronic Nanobubble Ultrasound Contrast Agents, 2010 Society of Biomaterials Annual Meeting, Seattle, Washington - *Poster presentation.*

76. Solorio L, Babbin BM, Patel R, Mach J, **Exner AA**. Characterization of In situ Forming Implants Using Ultrasound. Regional Conference, Society for Biomaterials, 9/25/2009, *selected oral presentation (and poster)*

77. Wilson R, Krupka TM, Solorio L, Wu H, **Exner AA.** Formulation and Characterization of Echogenic Lipid-Copolymer Nanobubbles. Regional Conference, Society for Biomaterials, 9/25/2009, *selected oral presentation (and poster)*

78. Carlson A, Patel R, **Exner AA.** Phase Inversion of Spherical PLGA Implants. Regional Conference, Society for Biomaterials, 9/25/2009, *poster presentation*

79. Krupka TM, Bederman I, Dremann D, **Exner AA**. Pluronic Triblock Copolymers Enhance Low Grade Hyperthermic Tumor Cell Injury. Society for Biomaterials Meeting, 4/22/2009, *poster presentation.*

80. Patel R, Solorio L, Carlson A, **Exner AA**. Characterization of formulation parameters affecting low molecular weight drug release from in situ forming drug delivery systems. Society for Biomaterials Annual Meeting, 4/22/2009, *poster presentation.*

81. Dremann D, Krupka Tm, Broome AM, **Exner AA**. Pluronic Activity in Hyperthermia-induced Tumor Cell Death. Society for Biomaterials Annual Meeting, 4/22/2009, *poster presentation.*

82. Solorio L, Babbin BM, Patel R, **Exner AA**. Reproducible Noninvasive Characterization of In Situ Forming Implants Using Ultrasound Society for Biomaterials Annual Meeting, 4/22/2009, *poster presentation.*

83. Zhang Y, Krupka TM, Wu H, **Exner AA.** Early Differentiation of Tumor and Inflammation Following Radiofrequency Ablation Using Contrast-enhanced Ultrasound, 2008 Radiological Society of North America (RSNA) meeting. *Oral presentation in 2 sessions*

84. Wu H, Krupka TM, **Exner AA,** Haaga JR. Perfusion Change after Radiofrequency Ablation of a Subcutaneous Tumor: Evaluated with Functional CT. 2008 Radiological Society of North America (RSNA) meeting. ***Research Fellow Award winner*.**

85. Wu H, **Exner AA**, Krupka TM, Weinberg BD, Haaga JR. Radiofrequency ablation: Effect of tumor blood flow modulation by vasoactive drugs and chemotherapy on coagulation size in a rat subcutaneous tumor model. Podium presentation at 2007 Radiological Society of North America (RSNA) meeting. ***Research Fellow Award winner***.

86. Krupka TM, Weinberg B, Wu H, **Exner AA**, "Dual Function of Pluronic P85 in Treatment of Experimental Carcinoma in Rat". Poster presentation at the 2007 Controlled Release Society annual meeting

87. Krupka TM, Weinberg B, Haaga JR, **Exner AA.** Thermosensitizer for Hyperthermic Treatment of Tumors, Poster presentation at the Society for Biomaterials 2007 annual meeting.

88. Nour S., Exner A, Wu H, Haaga J., Use of Vasoactive Drugs to Facilitate RF Ablation in a Rat Model. Society of Computed Body Tomography and Magnetic Resonance annual meeting; March 2007; Cum Laude Award for outstanding scientific paper.

89. Krupka TM, Weinberg B, Haaga JR, **Exner AA.** Thermosensitizer for Hyperthermic Treatment of Tumors, Poster presentation at the 2007 CWRU Research ShowCase. ***1st Prize Winner***.

90. Weinberg BW, Patel R, **Exner AA**, Saidel G, Gao J. "Estimating Local Doxorubicin Transport Properties of Experimental Liver Carcinoma". Poster presentation at the Society for Biomaterials 2007 annual meeting.

91. Patel R, Weinberg BW, Gao J , **Exner AA**, Saidel G. "Analyzing Intratumoral Chemotherapeutic Drug Penetration in Ablated Tumors Using Finite Element Methods". Oral presentation at the Society for Biomaterials 2007 annual meeting.

92. Krupka TM, Weinberg B, Haaga JR, **Exner AA. "**Intralesional chemotherapy depot improves outcome of radiofrequency ablation in experimental carcinoma." Oral presentation at the Radiological Society of North America (RSNA) meeting, November 2006.

93. Krupka TM, Weinberg B, Haaga JR, **Exner AA. "**Intravenous thermosensitizer administration improves outcome of radiofrequency ablation in experimental carcinoma model". Oral presentation at the Radiological Society of North America (RSNA) meeting, November 2006.

94. **Exner AA.** Research material presented in Basillion J, "Molecular Imaging in Cancer", invited talk, Nanotech 2006 Conference of the Nano Science and Technology Institute, May 2006.

95. Weinberg B, Blanco E, Lempka S, Anderson J, **Exner A**, Gao J. **"**RF ablation with adjuvant doxorubicin-eluting polymer implants for treatment of experimental liver tumors". 2006 Irwin H. Lepow Medical Student Research Day ***Poster Presentation Award winner***.

96. Weinberg B, Blanco E, Lempka S, Anderson J, **Exner A**, Gao J. **"**Radiofrequency ablation with adjuvant doxorubicin-eluting polymer implants for treatment of experimental liver tumors". Case Research Showcase, April 2006.

97. Haaga JR, **Exner AA**, Siegel C, Post A, Nakamoto DA. „Improved CT Differential Enhancement of Tumor from Normal Liver based using a Vasodilator to Change Angiogenic Blood Flow". American Hepato-Pancreato-Biliary Association annual meeting, March, 2006.

98. **Exner AA**, "Image-guided Radiofrequency Ablation and Local Chemotherapy", National Institute of Biomedical Imaging and Bioengineering Annual Meeting, Washington D.C., August 8-9, 2005.

99. Krupka T, Scherrer K, Teets JM, **Exner AA**, "Pluronic P85 Improves Efficacy of Intratumoral Carboplatin Treatment", Controlled Release Society Annual Meeting, June 2005.

100. Mehandru S, Hillenbrand C, **Exner AA**, "MRI Properties of Thermosensitive Pluronic Copolymers", Case Research Showcase, April 2005.

101. Krupka T, Scherrer K, **Exner AA**, "Pluronic-enhanced Intratumoral Chemotherapy", Case Research Showcase, April 2005.

102. Mehandru S, Hillenbrand C, **Exner AA**, "MRI Properties of Pluronic Triblock Copolymers", School of Medicine Lepow Research Day, March 2005, ***Student Award winner***

103. Scherrer K, Krupka T, Teets M, **Exner AA**, "Enhancement of carboplatin toxicity by Pluronic® block copolymers", Case Western Reserve University, Department of Biomedical Engineering, Undergraduate Senior Project Symposium, December 2004.

104. Smoke J, Krupka T, **Exner AA**, "Sensitization of cancer cells to hyperthermia-induced toxicity using Pluronic® block copolymers", Case Western Reserve University, Department of Biomedical Engineering, Undergraduate Senior Project Symposium, December 2004.

105. **Exner AA**, Dhande OS, Krupka TM, Stowe NT, Haaga JR, "Quantitative CT for imaging of site-specific drug delivery", oral presentation , Radiological Society of North America (RSNA), 2004.

106. **Exner AA**, Dhande OS, Stowe NT, Haaga JR, "Quantitative computed tomography imaging of site-specific drug delivery", poster presentation, American Association of Pharmaceutical Scientists (AAPS), 2004.

107. Scherrer K, Krupka T, Teets M, **Exner AA**, "Enhancement of carboplatin toxicity by Pluronic® block copolymers", New Jersey Symposium on Biomaterials Science, Somerset NJ, October 2004, ***Undergraduate Student Award Winner***

108. Dhande OS, **Exner AA,** "Formulation and Characterization of Drug-Loaded Injectable Polymers for Local Chemotherapy", Case Western Reserve University, Department of Biomedical Engineering, Undergraduate Senior Project Symposium, May 2004.

109. Weinberg B, **Szymanski-Exner AA**, Stowe NT, Gallacher A, Wilson DL, Haaga JR, Gao J, "Noninvasive Monitoring of Local Drug Release using X-ray Computed Tomography", Controlled Release Society, June 2004.

110. **Exner AA**, "Image Guided Drug Delivery", Image-Guided Interventions, a combined NIH, NASA and NSF Workshop, Bethesda MD May 13-14, 2004.

111. **Exner AA**, Stowe NT, Bhatt S, Haaga JR. "Functional CT Imaging of Blood Flow Changes During Tumor Development", Case Western Reserve University Research Showcase, April 2, 2004.

112. Weinberg B, **Exner AA,** Stowe NT, Gallacher A, Wilson DL, Haaga JR, Gao J. "Noninvasive Monitoring of Local Carboplatin Release using X-ray Computed Tomography", Case Western Reserve University Research Showcase, April 2, 2004.

113. Haaga JR, Exner AA, Ciancibello L, Smith D, Pohlman S, Stowe NT, "Functional CT Monitoring of Tumor Blood Supply During Development and After Radiofrequency Ablation and Local 5-FU Chemotherapy in an Experimental Model", Radiological Society of North America, Chicago IL, December 2003.

114. **Szymanski-Exner A**, Gallacher A, Stowe N, Weinberg B, Haaga J, Gao J, "Local Carboplatin Delivery and Tissue Distribution in Livers Following Radiofrequency (RF) Ablation", presented at Society for Biomaterials Meeting, Reno NV, 2003.

115. Weinberg BD, **Exner AA**, Stowe NT, Lazebnik RS, Wilson DL, Gao J, "Noninvasive Monitoring of Local Carboplatin Release using X-ray Computed Tomography", Biomedical Engineering Society Annual Meeting, Nashville TN, October, 2003.

116. **Szymanski-Exner A**, Stowe NT, Gallacher A, Weinberg B, Haaga JR, Gao J, "Local carboplatin delivery to livers following radiofrequency (RF) thermal ablation", poster presentation at the 6th New Jersey Symposium on Biomaterials Science Somerset NJ, October 2002, **Student Award Winner.**

117. Szymanski-Exner A, Stowe NT, Lazebnik R, Haaga JR, Gao J, "Non-Invasive Monitoring of Drug Release from a Biodegradable PLGA Implant Using X-ray Computed Tomography: An In Vivo/In Vitro Correlation", podium presentation at the 2002 Society for Biomaterials meeting, Tampa FL, **Student Award Winner.**

118. Gao J, Qian F, **Szymanski-Exner A**, Stowe N, Haaga J, Comparison of Drug Distribution Profiles in Thermoablated and Normal Rabbit Livers In Vivo. Society for Biomaterials meeting, Tampa, FL, 2002.

119. Gao J, **Szymanski-Exner A**, Stowe N, Haaga J, Monitoring Carboplatin Release and Distribution in vivo by Computed Tomography, BMES meeting, 2001.

120. Gao J, **Szymanski-Exner A**, Stowe N, Haaga J, Monitoring Drug Release and Distribution in vivo by Computed Tomography, ASME Summer Bioengineering Conference, 2001.

121. **Szymanski A**, Stowe N, Haaga JR, Gao J, "Development of computed tomography as a non-invasive method of quantifying drug release and distribution in vivo", poster presentation at the CWRU Biomedical Engineering Research Day, February 2001

122. Qian F, **Szymanski A**, Gao J, Controlled Release PLGA Millirods for Intratumoral Drug Delivery, Society for Biomaterials, 2000.

123. **Szymanski AA**, Stowe N, Haaga JR, Gao J, "Development of computed tomography as a non-invasive method of quantifying drug release and distribution in vivo", poster presentation at the Biomedical Engineering Society Annual Meeting, Seattle WA, October, 2000

124. **Szymanski AA**, Haaga JR, Stowe N, Basile V, Wilson DL, Salem KA, Gao J, "Fabrication and Characterization of Poly(lactide-co-glycolide) Millirods for Controlled Drug Delivery", Society for Biomaterials World Congress, 2000.

125. Szymanski AA, Stowe N, Haaga JR, Gao J, "Poly(D,L-lactide-co-glycolide) Millirods for Controlled Drug Delivery to Thermally Ablated Liver Tissue", oral presentation at the CWRU BME Research Day, 2000